

CHAPTER

3



Acids and Bases

AN INTRODUCTION TO ORGANIC REACTIONS AND THEIR MECHANISMS

To the uninitiated, a chemical reaction must seem like an act of magic. A chemist puts one or two reagents into a flask, waits for a time, and then takes from the flask one or more completely different compounds. It is, until we understand the details of the reaction, like a magician who puts apples and oranges in a hat, shakes it, and then pulls out rabbits and parakeets. We see a real-life example of this sort of “magic” in the photo above, where a strand of solid nylon is being pulled from a flask that contains two immiscible solutions. This synthesis of nylon is not magic, but it is indeed wonderful and amazing, and reactions like it have transformed our world.

One of our goals in this course will be, in fact, to try to understand how this chemical magic takes place. We will want to be able to explain *how the products of the reaction are formed*. This explanation will take the form of a **reaction mechanism**—a description of the events that take place on a molecular level as reactants become products. If, as is often the case, the reaction takes place in more than one step, we will want to know what chemical species, called **intermediates**, intervene between each step along the way.

One of the most important things about using mechanisms to learn organic chemistry is this: mechanisms help us organize what otherwise might be an overwhelmingly complex body of knowledge into a form that makes it understandable. There are millions of organic compounds now known, and there are millions of reactions that these compounds undergo. If we had to learn them all by rote memorization, then we would soon give up. But, we don't have to do this. In the same way

that functional groups help us organize compounds in a comprehensible way, mechanisms help us organize reactions. Fortunately, too, there are a relatively small number of basic mechanisms.

IN THIS CHAPTER WE WILL CONSIDER:

- rules that show how to classify reactive groups within molecules from the standpoints of acids and bases as well as from electron-rich and electron-poor domains
- the step-by-step processes of a chemical reaction and how to codify these processes into a few specific, easy-to-understand types

[WHY DO THESE TOPICS MATTER?] At the end of the chapter, we will show a rare case where an important discovery that truly changed the world was made without any knowledge of these principles. However, the rare occurrence of such events argues for why real advances require a core understanding of the topics in this chapter.

3.1 ACID–BASE REACTIONS

We begin our study of chemical reactions and mechanisms by examining some of the basic principles of acid–base chemistry. There are several reasons for doing this:

- Many of the reactions that occur in organic chemistry are either acid–base reactions themselves or they involve an acid–base reaction at some stage.
- Acid–base reactions are simple fundamental reactions that will enable you to see how chemists use curved arrows to represent mechanisms of reactions and how they depict the processes of bond breaking and bond making that occur as molecules react.

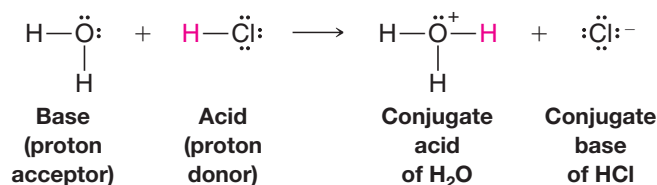
3.1A Brønsted–Lowry Acids and Bases

Two classes of acid–base reactions are fundamental in organic chemistry: Brønsted–Lowry and Lewis acid–base reactions. We start our discussion with Brønsted–Lowry acid–base reactions.

- **Brønsted–Lowry acid–base** reactions involve the transfer of protons.
- A **Brønsted–Lowry acid** is a substance that can donate (or lose) a proton.
- A **Brønsted–Lowry base** is a substance that can accept (or remove) a proton.

Let us consider some examples.

Hydrogen chloride (HCl), in its pure form, is a gas. When HCl gas is bubbled into water, the following reaction occurs.



In this reaction hydrogen chloride donates a proton; therefore it acts as a Brønsted–Lowry acid. Water accepts a proton from hydrogen chloride; thus water serves as a Brønsted–Lowry base. The products are a hydronium ion (H_3O^+) and chloride ion (Cl^-).

Just as we classified the reactants as either an acid or a base, we also classify the products in a specific way.

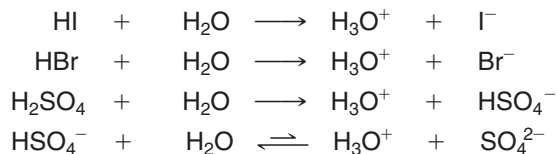
- The molecule or **ion** that forms when an acid loses its proton is called the **conjugate base** of that acid. In the above example, chloride ion is the conjugate base.
- The molecule or ion that forms when a base accepts a proton is called the **conjugate acid**. Hydronium ion is the conjugate acid of water.



The color of hydrangea flowers depends, in part, on the relative acidity of their soil.



Hydrogen chloride is considered a strong acid because transfer of its proton in water proceeds essentially to completion. Other strong acids that completely transfer a proton when dissolved in water are hydrogen iodide, hydrogen bromide, and sulfuric acid.



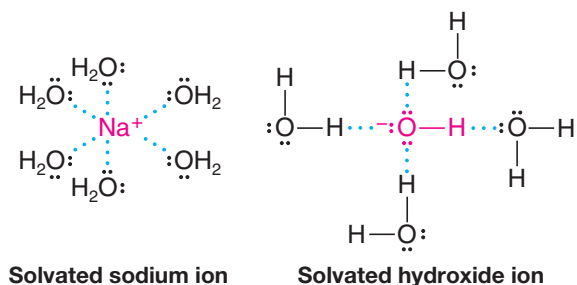
- The extent to which an acid transfers protons to a base, such as water, is a measure of its strength as an acid. Acid strength is therefore a measure of the percentage of ionization and *not* of concentration.

Sulfuric acid is called a diprotic acid because it can transfer two protons. Transfer of the first proton occurs completely, while the second is transferred only to the extent of about 10% (hence the equilibrium arrows in the equation for the second proton transfer).

3.1B Acids and Bases in Water

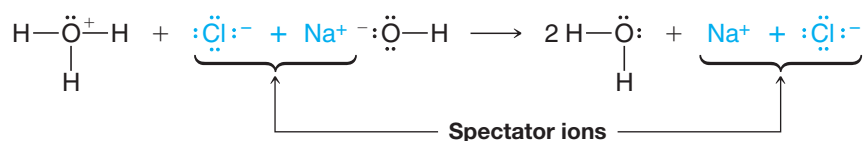
- Hydronium ion is the strongest acid that can exist in water to any significant extent. Any acid stronger than hydronium ion will simply transfer its proton to a water molecule to form hydronium ions.
- Hydroxide ion is the strongest base that can exist in water to any significant extent. Any base stronger than hydroxide will remove a proton from water to form hydroxide ions.

When an ionic compound dissolves in water the ions are solvated. With sodium hydroxide, for example, the positive sodium ions are stabilized by interaction with unshared electron pairs of water molecules, and the hydroxide ions are stabilized by hydrogen bonding of their unshared electron pairs with the partially positive hydrogens of water molecules.

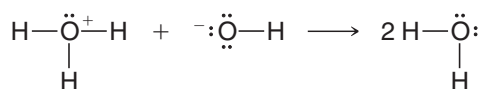


When an aqueous solution of sodium hydroxide is mixed with an aqueous solution of hydrogen chloride (hydrochloric acid), the reaction that occurs is between hydronium and hydroxide ions. The sodium and chloride ions are called **spectator ions** because they play no part in the acid–base reaction:

Total Ionic Reaction



Net Reaction



What we have just said about hydrochloric acid and aqueous sodium hydroxide is true when solutions of all aqueous strong acids and bases are mixed. The net **ionic reaction** is simply



3.2 HOW TO USE CURVED ARROWS IN ILLUSTRATING REACTIONS

Up to this point we have not indicated how bonding changes occur in the reactions we have presented, but this can easily be done using curved-arrow notation. **Curved arrows** show the direction of electron flow in a reaction mechanism.

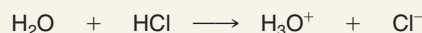
1. Draw the curved arrow so that it points from the source of an electron pair to the atom receiving the pair. (Curved arrows can also show the movement of single electrons. We shall discuss reactions of this type in a later chapter.)
2. Always show the flow of electrons from a site of higher electron density to a site of lower electron density.
3. **Never** use curved arrows to show the movement of atoms. Atoms are assumed to follow the flow of the electrons.
4. Make sure that the movement of electrons shown by the curved arrow does not violate the octet rule for elements in the second row of the periodic table.

The reaction of hydrogen chloride with water provides a simple example of how to use curved arrow notation. Here we invoke the first of many “A Mechanism for the Reaction” boxes, in which we show every key step in a mechanism using color-coded formulas accompanied by explanatory captions.

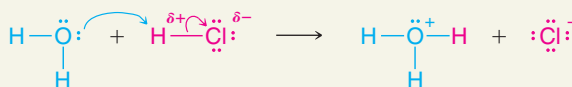
A MECHANISM FOR THE REACTION

Reaction of Water with Hydrogen Chloride: The Use of Curved Arrows

Reaction



Mechanism



A water molecule uses one of the nonbonding electron pairs to form a bond to a proton of HCl. The bond between the hydrogen and chlorine breaks, and the electron pair goes to the chlorine atom.

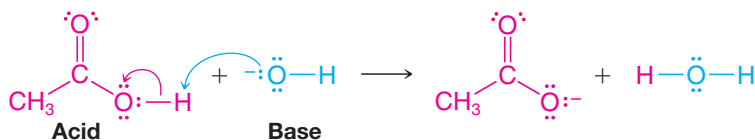
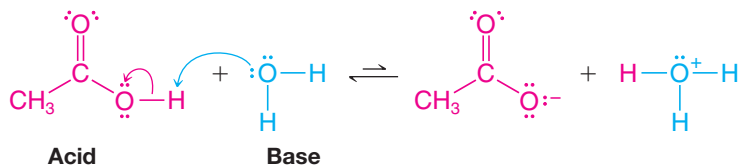
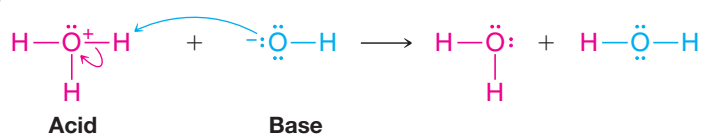
This leads to the formation of a hydronium ion and a chloride ion.

Helpful Hint

Curved arrows point *from* electrons to the atom receiving the electrons.

The curved arrow begins with a covalent bond or unshared electron pair (a site of higher electron density) and points toward a site of electron deficiency. We see here that as the water molecule collides with a hydrogen chloride molecule, it uses one of its unshared electron pairs (shown in blue) to form a bond to the proton of HCl. This bond forms because the negatively charged electrons of the oxygen atom are attracted to the positively charged proton. As the bond between the oxygen and the proton forms, the hydrogen–chlorine bond of HCl breaks, and the chlorine of HCl departs with the electron pair that formerly bonded it to the proton. (If this did not happen, the proton would end up forming two covalent bonds, which, of course, a proton cannot do.) We, therefore, use a curved arrow to show the bond cleavage as well. By pointing from the bond to the chlorine, the arrow indicates that the bond breaks and the electron pair leaves with the chloride ion.

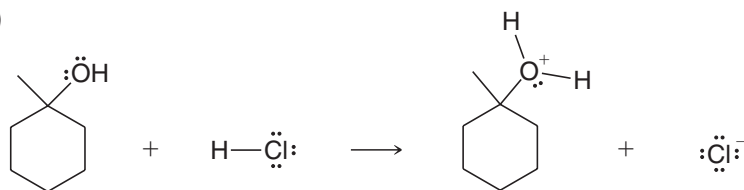
The following acid–base reactions give other examples of the use of the curved-arrow notation:



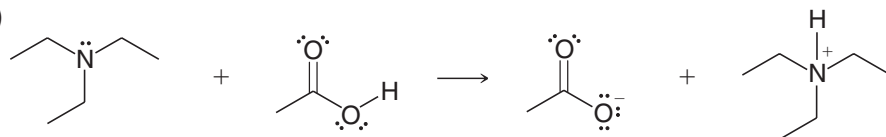
SOLVED PROBLEM 3.1

Add curved arrows to the following reactions to indicate the flow of electrons for all of the bond-forming and bond-breaking steps.

(a)



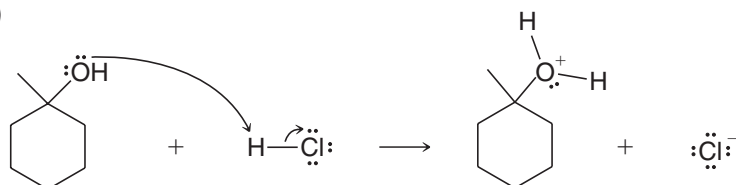
(b)



STRATEGY AND ANSWER: Recall the rules for use of curved arrows presented at the beginning of Section 3.2. Curved arrows point from the source of an electron pair to the atom receiving the pair, and always point from a site of higher electron density to a site of lower electron density. We must also not exceed two electrons for a hydrogen atom, or an octet of electrons for any elements in the second row of the periodic table. We must also account for the formal charges on atoms and write equations whose charges are balanced.

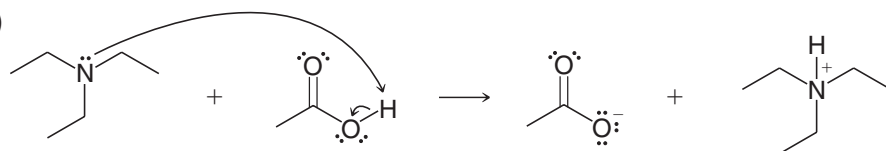
In (a), the hydrogen atom of HCl is partially positive (electrophilic) due to the electronegativity of the chlorine atom. The alcohol oxygen is a source of electrons (a Lewis base) that can be given to this partially positive proton. The proton must lose a pair of electrons as it gains a pair, however, and thus the chloride ion accepts a pair of electrons from the bond it had with the hydrogen atom as the hydrogen becomes bonded to the alcohol oxygen.

(a)

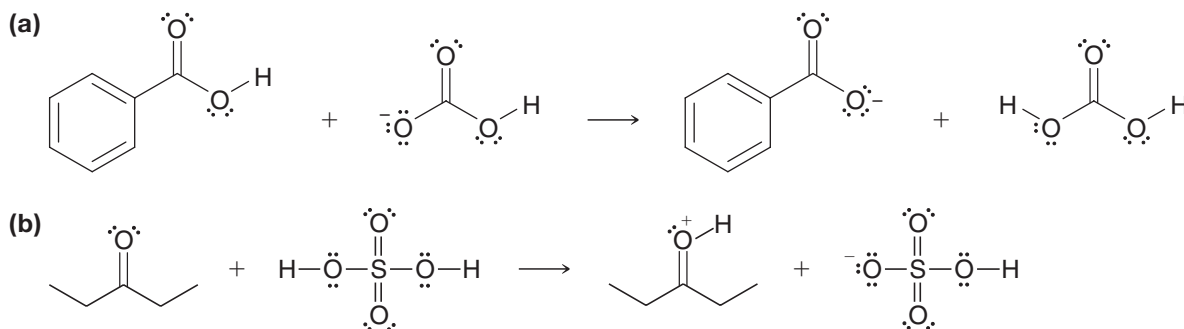


In (b), the carboxylic acid hydrogen is partially positive and therefore electrophilic, and the amine provides an unshared pair of electrons that forms a bond with the carboxylic acid hydrogen, causing departure of a carboxylate anion.

(b)



Add curved arrows to the following reactions to indicate the flow of electrons for all of the bond-forming and bond-breaking steps.

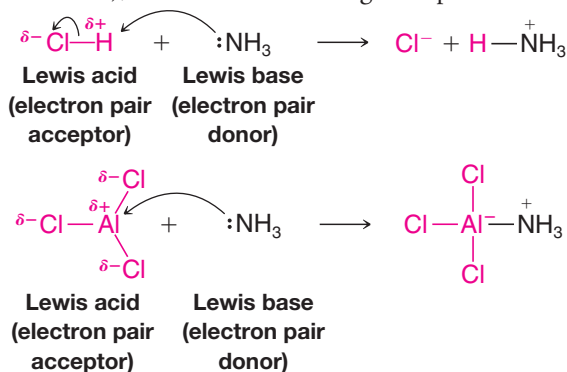
PRACTICE PROBLEM 3.1


3.3 LEWIS ACIDS AND BASES

In 1923 G. N. Lewis proposed a theory that significantly broadened the understanding of acids and bases. As we go along we shall find that an understanding of **Lewis acid–base theory** is exceedingly helpful to understanding a variety of organic reactions. Lewis proposed the following definitions for acids and bases.

- Acids are electron pair acceptors.
- Bases are electron pair donors.

In Lewis acid–base theory, proton donors are not the only acids; many other species are acids as well. Aluminum chloride, for example, reacts with ammonia in the same way that a proton donor does. Using curved arrows to show the donation of the electron pair of ammonia (the Lewis base), we have the following examples:



In the reaction with hydrogen chloride above, notice that the electron pair acceptor (the proton) must also lose an electron pair as the new bond is formed with nitrogen. This is necessary because the hydrogen atom had a full valence shell of electrons at the start. On the other hand, because the valence shell of the aluminum atom in aluminum chloride was not full at the beginning (it had only a sextet of valence electrons), it can accept an electron pair without breaking any bonds. The aluminum atom actually achieves an octet by accepting the pair from nitrogen, although it gains a formal negative charge. When it accepts the electron pair, aluminum chloride is, in the Lewis definition, *acting as an acid*.

Bases are much the same in the Lewis theory and in the Brønsted–Lowry theory, because in the Brønsted–Lowry theory a base must donate a pair of electrons in order to accept a proton.

- The Lewis theory, by virtue of its broader definition of acids, allows acid–base theory to include all of the Brønsted–Lowry reactions and, as we shall see, a great many others. Most of the reactions we shall study in organic chemistry involve Lewis acid–base interactions, and a sound understanding of Lewis acid–base chemistry will help greatly.

Helpful Hint

Verify for yourself that you can calculate the formal charges in these structures.


Carbonic anhydrase

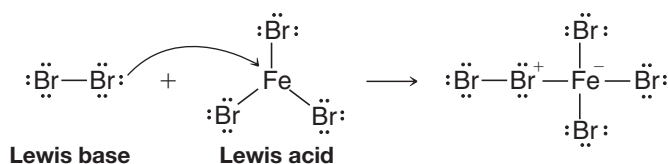
A zinc ion acts as a Lewis acid in the mechanism of the enzyme carbonic anhydrase (Chapter 24).

Any *electron-deficient atom* can act as a Lewis acid. Many compounds containing group IIIA elements such as boron and aluminum are Lewis acids because group IIIA atoms have only a sextet of electrons in their outer shell. Many other compounds that have atoms with vacant orbitals also act as Lewis acids. Zinc and iron(III) halides (ferric halides) are frequently used as Lewis acids in organic reactions.

SOLVED PROBLEM 3.2

Write an equation that shows the Lewis acid and Lewis base in the reaction of bromine (Br_2) with ferric bromide (FeBr_3).

ANSWER:



3.3A Opposite Charges Attract

- In Lewis acid–base theory, as in many organic reactions, the attraction of oppositely charged species is fundamental to reactivity.

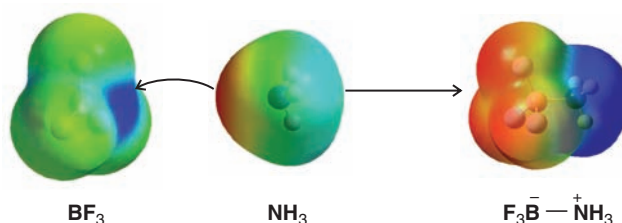
As one further example, we consider boron trifluoride, an even more powerful Lewis acid than aluminum chloride, and its reaction with ammonia. The calculated structure for boron trifluoride in Fig. 3.1 shows electrostatic potential at its van der Waals surface (like that in Section 2.2A for HCl). It is obvious from this figure (and you should be able to predict this) that BF_3 has substantial positive charge centered on the boron atom and negative charge located on the three fluorines. (The convention in these structures is that blue represents relatively positive areas and red represents relatively negative areas.) On the other hand, the surface electrostatic potential for ammonia shows (as you would expect) that substantial negative charge is localized in the region of ammonia's nonbonding electron pair. Thus, the electrostatic properties of these two molecules are perfectly suited for a Lewis acid–base reaction. When the expected reaction occurs between them, the nonbonding electron pair of ammonia attacks the boron atom of boron trifluoride, filling boron's valence shell. The boron now carries a formal negative charge and the nitrogen carries a formal positive charge. This separation of charge is borne out in the electrostatic potential map for the product shown in Fig. 3.1. Notice that substantial negative charge resides in the BF_3 part of the molecule, and substantial positive charge is localized near the nitrogen.

Helpful Hint

The need for a firm understanding of structure, formal charges, and electronegativity can hardly be emphasized enough as you build a foundation of knowledge for learning organic chemistry.

Although calculated electrostatic potential maps like these illustrate charge distribution and molecular shape well, it is important that you are able to draw the same conclusions based on what you would have predicted about the structures of BF_3 and NH_3 and their reaction product using orbital hybridization (Sections 1.13–1.15), VSEPR models (Section 1.17), consideration of formal charges (Section 1.5), and electronegativity (Sections 1.3A and 2.2).

FIGURE 3.1 Electrostatic potential maps for BF_3 and NH_3 and the product that results from reaction between them. Attraction between the strongly positive region of BF_3 and the negative region of NH_3 causes them to react. The electrostatic potential map for the product shows that the fluorine atoms draw in the electron density of the formal negative charge, and the nitrogen atom, with its hydrogens, carries the formal positive charge.



Write equations showing the Lewis acid–base reaction that takes place when:

PRACTICE PROBLEM 3.2

- (a) Methanol (CH_3OH) reacts with BF_3 .
 (b) Chloromethane (CH_3Cl) reacts with AlCl_3 .
 (c) Dimethyl ether (CH_3OCH_3) reacts with BF_3 .

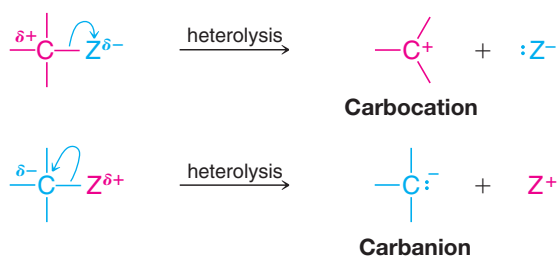
Which of the following are potential Lewis acids and which are potential Lewis bases?

PRACTICE PROBLEM 3.3

- (a) $\text{CH}_3\text{CH}_2\text{-}\overset{\text{N}}{\underset{\text{CH}_3}{|}}{\text{CH}_3}$ (c) $(\text{C}_6\text{H}_5)_3\text{P:}$ (e) $(\text{CH}_3)_3\text{B}$
 (b) $\text{H}_3\text{C-C}^+\begin{matrix} \text{CH}_3 \\ | \\ \text{CH}_3 \end{matrix}$ (d) $:\ddot{\text{Br}}:^-$ (f) H^-

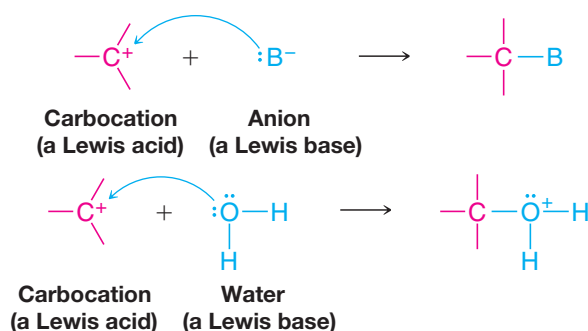
3.4 HETEROLYSIS OF BONDS TO CARBON: CARBOCATIONS AND CARBANIONS

Heterolysis of a bond to a carbon atom can lead to either of two ions: either to an ion with a positive charge on the carbon atom, called a **carbocation**, or to an ion with a negatively charged carbon atom, called a **carbanion**:



- Carbocations are electron deficient. They have only six electrons in their valence shell, and because of this, carbocations are Lewis acids.

In this way they are like BF_3 and AlCl_3 . Most carbocations are also short-lived and highly reactive. They occur as intermediates in some organic reactions. Carbocations react rapidly with Lewis bases—with molecules or ions that can donate the electron pair that they need to achieve a stable octet of electrons (i.e., the electronic configuration of a noble gas):

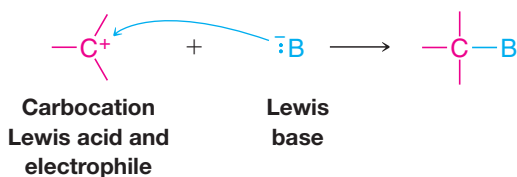


- **Carbanions** are electron rich. They are anions and have an unshared electron pair. Carbanions, therefore, are **Lewis bases and react accordingly** (Section 3.3).

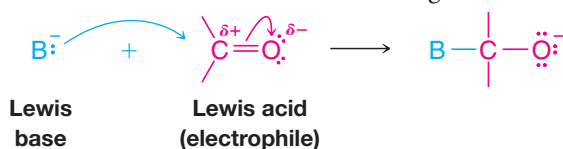
3.4A Electrophiles and Nucleophiles

Because carbocations are *electron-seeking reagents* chemists call them **electrophiles** (meaning electron-loving).

- **Electrophiles** are reagents that seek electrons so as to achieve a stable shell of electrons like that of a noble gas.
- All Lewis acids are electrophiles. By accepting an electron pair from a Lewis base, a carbocation fills its valence shell.



- Carbon atoms that are electron poor because of bond polarity, but are not carbocations, can also be electrophiles. They can react with the electron-rich centers of Lewis bases in reactions such as the following:

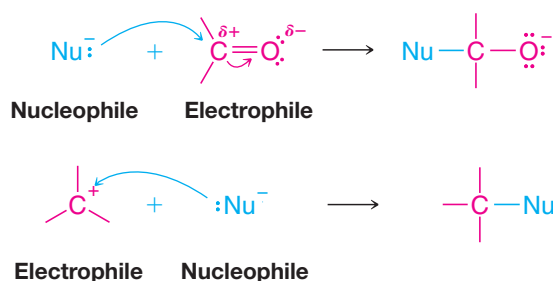


Carbanions are Lewis bases. Carbanions seek a proton or some other positive center to which they can donate their electron pair and thereby neutralize their negative charge.

When a Lewis base *seeks a positive center other than a proton, especially that of a carbon atom*, chemists call it a **nucleophile** (meaning nucleus loving; the *nucleo-* part of the name comes from *nucleus*, the positive center of an atom).

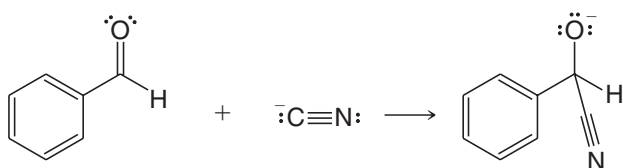
- A **nucleophile** is a Lewis base that seeks a positive center such as a positively charged carbon atom.

Since electrophiles are also Lewis acids (electron pair acceptors) and nucleophiles are Lewis bases (electron pair donors), why do chemists have two terms for them? The answer is that *Lewis acid* and *Lewis base* are terms that are used generally, but when one or the other reacts to form a bond to a carbon atom, we usually call it an *electrophile* or a *nucleophile*.

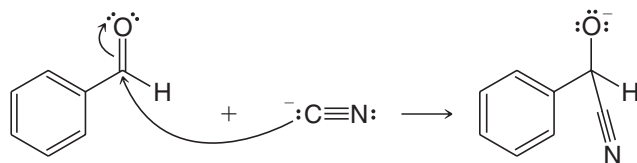


SOLVED PROBLEM 3.3

Identify the electrophile and the nucleophile in the following reaction, and add curved arrows to indicate the flow of electrons for the bond-forming and bond-breaking steps.



STRATEGY AND ANSWER: The aldehyde carbon is electrophilic due to the electronegativity of the carbonyl oxygen. The cyanide anion acts as a Lewis base and is the nucleophile, donating an electron pair to the carbonyl carbon, and causing an electron pair to shift to the oxygen so that no atom has more than an octet of electrons.



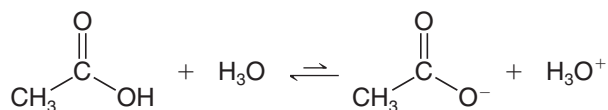
Use the curved-arrow notation to write the reaction that would take place between dimethylamine $(\text{CH}_3)_2\text{NH}$ and boron trifluoride. Identify the Lewis acid, Lewis base, nucleophile, and electrophile and assign appropriate formal charges.

PRACTICE PROBLEM 3.4

3.5 THE STRENGTH OF BRØNSTED-LOWRY ACIDS AND BASES: K_a AND pK_a

Many organic reactions involve the transfer of a proton by an acid–base reaction. An important consideration, therefore, is the relative strengths of compounds that could potentially act as Brønsted–Lowry acids or bases in a reaction.

In contrast to the strong acids, such as HCl and H_2SO_4 , acetic acid is a much weaker acid. When acetic acid dissolves in water, the following reaction does not proceed to completion:



Experiments show that in a 0.1 M solution of acetic acid at 25 °C only about 1% of the acetic acid molecules ionize by transferring their protons to water. Therefore, acetic acid is a weak acid. As we shall see next, **acid strength** is characterized in terms of **acidity constant** (K_a) or pK_a values.

3.5A The Acidity Constant, K_a

Because the reaction that occurs in an aqueous solution of acetic acid is an equilibrium, we can describe it with an expression for the **equilibrium constant** (K_{eq}):

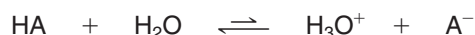
$$K_{\text{eq}} = \frac{[\text{H}_3\text{O}^+][\text{CH}_3\text{CO}_2^-]}{[\text{CH}_3\text{CO}_2\text{H}][\text{H}_2\text{O}]}$$

For dilute aqueous solutions, the concentration of water is essentially constant (~ 55.5 M), so we can rewrite the expression for the equilibrium constant in terms of a new constant (K_a) called the **acidity constant**:

$$K_a = K_{\text{eq}}[\text{H}_2\text{O}] = \frac{[\text{H}_3\text{O}^+][\text{CH}_3\text{CO}_2^-]}{[\text{CH}_3\text{CO}_2\text{H}]}$$

At 25 °C, the acidity constant for acetic acid is 1.76×10^{-5} .

We can write similar expressions for any weak acid dissolved in water. Using a generalized hypothetical acid (HA), the reaction in water is



and the expression for the acidity constant is

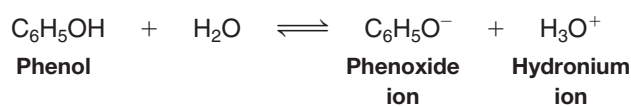
$$K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]}$$

Because the concentrations of the products of the reaction are written in the numerator and the concentration of the undissociated acid in the denominator, **a large value of K_a means the acid is a strong acid and a small value of K_a means the acid is a weak acid.** If the K_a is greater than 10, the acid will be, for all practical purposes, completely dissociated in water at concentrations less than 0.01 M.

SOLVED PROBLEM 3.4

Phenol ($\text{C}_6\text{H}_5\text{OH}$) has $K_a = 1.26 \times 10^{-10}$. **(a)** What is the molar concentration of hydronium ion in a 1.0 M solution of phenol? **(b)** What is the pH of the solution?

STRATEGY AND ANSWER: Use the equation for K_a for the equilibrium:



$$K_a = \frac{[\text{H}_3\text{O}^+][\text{C}_6\text{H}_5\text{O}^-]}{[\text{C}_6\text{H}_5\text{OH}]} = 1.26 \times 10^{-10}$$

At equilibrium the concentration of hydronium ion will be the same as that of phenoxide ion, thus we can let them both equal x . Therefore

$$\frac{(x)(x)}{1.0} = \frac{x^2}{1.0} = 1.26 \times 10^{-10}$$

and

$$x = 1.1 \times 10^{-5}$$

PRACTICE PROBLEM 3.5 Formic acid (HCO_2H) has $K_a = 1.77 \times 10^{-4}$. **(a)** What are the molar concentrations of the hydronium ion and formate ion (HCO_2^-) in a 0.1 M aqueous solution of formic acid? **(b)** What percentage of the formic acid is ionized?

3.5B Acidity and $\text{p}K_a$

Chemists usually express the acidity constant, K_a , as its negative logarithm, $\text{p}K_a$:

$$\text{p}K_a = -\log K_a$$

This is analogous to expressing the hydronium ion concentration as pH:

$$\text{pH} = -\log[\text{H}_3\text{O}^+]$$

For acetic acid the $\text{p}K_a$ is 4.75:

$$\text{p}K_a = -\log(1.76 \times 10^{-5}) = -(-4.75) = 4.75$$

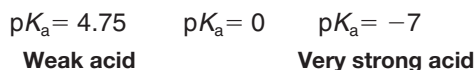
Notice that there is an inverse relationship between the magnitude of the $\text{p}K_a$ and the strength of the acid.

- **The larger the value of the $\text{p}K_a$, the weaker is the acid.**

For example, acetic acid with $\text{p}K_a = 4.75$ is a weaker acid than trifluoroacetic acid with $\text{p}K_a = 0$ ($K_a = 1$). Hydrochloric acid with $\text{p}K_a = -7$ ($K_a = 10^7$) is a far stronger acid than trifluoroacetic acid. (It is understood that a positive $\text{p}K_a$ is larger than a negative $\text{p}K_a$.)

Helpful Hint

K_a and $\text{p}K_a$ are indicators of acid strengths.



Increasing acid strength

Table 3.1 lists pK_a values for a selection of acids relative to water as the base.

TABLE 3.1 RELATIVE STRENGTH OF SELECTED ACIDS AND THEIR CONJUGATE BASES

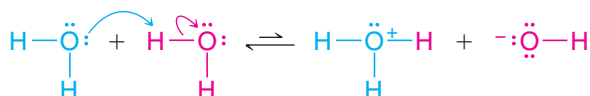
	Acid	Approximate pK_a	Conjugate Base	
Strongest acid	HSbF_6	< -12	SbF_6^-	Weakest base
	HI	-10	I^-	
	H_2SO_4	-9	HSO_4^-	
	HBr	-9	Br^-	
	HCl	-7	Cl^-	
	$\text{C}_6\text{H}_5\text{SO}_3\text{H}$	-6.5	$\text{C}_6\text{H}_5\text{SO}_3^-$	
	$(\text{CH}_3)_2\overset{+}{\text{O}}\text{H}$	-3.8	$(\text{CH}_3)_2\text{O}$	
	$(\text{CH}_3)_2\text{C}=\overset{+}{\text{O}}\text{H}$	-2.9	$(\text{CH}_3)_2\text{C}=\text{O}$	
	$\text{CH}_3\overset{+}{\text{O}}\text{H}_2$	-2.5	CH_3OH	
	H_3O^+	-1.74	H_2O	
	HNO_3	-1.4	NO_3^-	
	$\text{CF}_3\text{CO}_2\text{H}$	0.18	CF_3CO_2^-	
	HF	3.2	F^-	
	$\text{C}_6\text{H}_5\text{CO}_2\text{H}$	4.21	$\text{C}_6\text{H}_5\text{CO}_2^-$	
	$\text{C}_6\text{H}_5\text{NH}_3^+$	4.63	$\text{C}_6\text{H}_5\text{NH}_2$	
	$\text{CH}_3\text{CO}_2\text{H}$	4.75	CH_3CO_2^-	
	H_2CO_3	6.35	HCO_3^-	
	$\text{CH}_3\text{COCH}_2\text{COCH}_3$	9.0	$\text{CH}_3\text{CO}\overset{-}{\text{C}}\text{HCOCH}_3$	
	NH_4^+	9.2	NH_3	
	$\text{C}_6\text{H}_5\text{OH}$	9.9	$\text{C}_6\text{H}_5\text{O}^-$	
	HCO_3^-	10.2	CO_3^{2-}	
	CH_3NH_3^+	10.6	CH_3NH_2	
	H_2O	15.7	HO^-	
	$\text{CH}_3\text{CH}_2\text{OH}$	16	$\text{CH}_3\text{CH}_2\text{O}^-$	
	$(\text{CH}_3)_3\text{COH}$	18	$(\text{CH}_3)_3\text{CO}^-$	
	CH_3COCH_3	19.2	$\overset{-}{\text{C}}\text{H}_2\text{COCH}_3$	
	$\text{HC}\equiv\text{CH}$	25	$\text{HC}\equiv\text{C}^-$	
	$\text{C}_6\text{H}_5\text{NH}_2$	31	$\text{C}_6\text{H}_5\text{NH}^-$	
	H_2	35	H^-	
	$(i\text{-Pr})_2\text{NH}$	36	$(i\text{-Pr})_2\text{N}^-$	
	NH_3	38	$\overset{-}{\text{N}}\text{H}_2$	
	$\text{CH}_2=\text{CH}_2$	44	$\text{CH}_2=\text{CH}^-$	
Weakest acid	CH_3CH_3	50	CH_3CH_2^-	Strongest base

The values in the middle pK_a range of Table 3.1 are the most accurate because they can be measured in aqueous solution. Special methods must be used to estimate the pK_a values for the very strong acids at the top of the table and for the very weak acids at the bottom.* The pK_a values for these very strong and weak acids are therefore approximate. All of the acids that we shall consider in this book will have strengths in between that of ethane (an extremely weak acid) and that of HSbF_6 (an acid that is so strong that it is called a “superacid”). As you examine Table 3.1, take care not to lose sight of the vast range of acidities that it represents (a factor of 10^{62}).

*Acids that are stronger than a hydronium ion and bases that are stronger than a hydroxide ion react completely with water (a phenomenon called the **leveling effect**; see Sections 3.1B and 3.14). Therefore, it is not possible to measure acidity constants for these acids in water. Other solvents and special techniques are used, but we do not have the space to describe those methods here.

PRACTICE PROBLEM 3.6 (a) An acid (HA) has $K_a = 10^{-7}$. What is its pK_a ? (b) Another acid (HB) has $K_a = 5$. What is its pK_a ? (c) Which is the stronger acid?

Water, itself, is a very weak acid and undergoes self-ionization even in the absence of acids and bases:



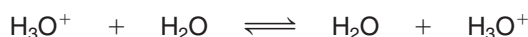
In pure water at 25 °C, the concentrations of hydronium and hydroxide ions are equal to 10^{-7} M. Since the concentration of water in pure water is 55.5 M, we can calculate the K_a for water.

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{OH}^-]}{[\text{H}_2\text{O}]} \quad K_a = \frac{(10^{-7})(10^{-7})}{55.5} = 1.8 \times 10^{-16} \quad pK_a = 15.7$$

SOLVED PROBLEM 3.5

Show calculations proving that the pK_a of the hydronium ion (H_3O^+) is -1.74 as given in Table 3.1.

STRATEGY AND ANSWER: When H_3O^+ acts as an acid in aqueous solution, the equilibrium is



and K_a is equal to the molar concentration of water;

$$K_a = \frac{[\text{H}_2\text{O}][\text{H}_3\text{O}^+]}{[\text{H}_3\text{O}^+]} = [\text{H}_2\text{O}]$$

The molar concentration of H_2O in pure H_2O is equal to the number of moles of H_2O (MW = 18 g/mol) in 1000 g (one liter) of water. That is, $[\text{H}_2\text{O}] = 1000 \text{ g L}^{-1}/18 \text{ g/mole}^{-1} = 55.5$. Therefore, $K_a = 55.5$. The $pK = -\log 55.5 = -1.74$.

3.5C Predicting the Strength of Bases

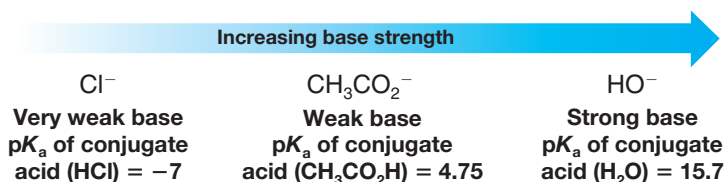
In our discussion so far we have dealt only with the strengths of acids. Arising as a natural corollary to this is a principle that allows us to estimate the **base strength**. Simply stated, the principle is this:

- The stronger the acid, the weaker will be its **conjugate base**.

We can, therefore, **relate the strength of a base to the pK_a of its conjugate acid**.

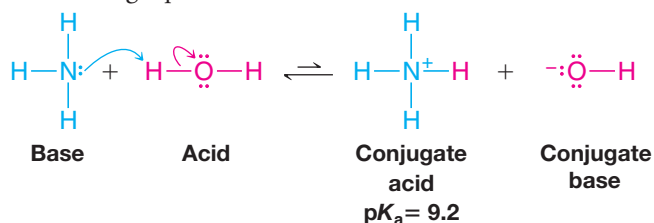
- The larger the pK_a of the conjugate acid, the stronger is the base.

Consider the following as examples:

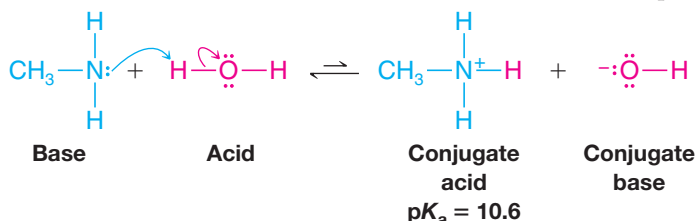


We see that the hydroxide ion is the strongest in this series of three bases because its conjugate acid, water, is the weakest acid. We know that water is the weakest acid because it has the largest pK_a .

Amines are like ammonia in that they are weak bases. Dissolving ammonia in water brings about the following equilibrium:



Dissolving methylamine in water causes the establishment of a similar equilibrium.

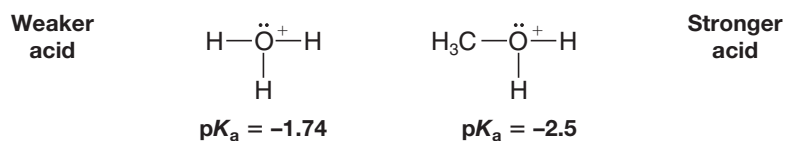


Again we can relate the basicity of these substances to the strength of their conjugate acids. The conjugate acid of ammonia is the ammonium ion, NH_4^+ . The pK_a of the ammonium ion is 9.2. The conjugate acid of methylamine is the CH_3NH_3^+ ion. This ion, called the methylaminium ion, has $pK_a = 10.6$. Since the conjugate acid of methylamine is a weaker acid than the conjugate acid of ammonia, we can conclude that methylamine is a stronger base than ammonia.

SOLVED PROBLEM 3.6

Using the pK_a values in Table 3.1 decide which is the stronger base, CH_3OH or H_2O .

STRATEGY AND ANSWER: From Table 3.1, we find the pK_a values of the conjugate acids of water and methanol.

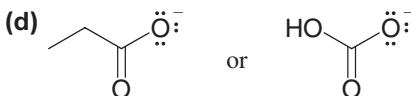
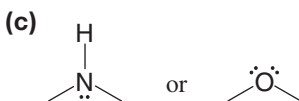
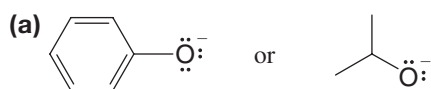


Because water is the conjugate base of the weaker acid, it is the stronger base.



Using the pK_a values of analogous compounds in Table 3.1, predict which would be the stronger base.

PRACTICE PROBLEM 3.7



SOLVED PROBLEM 3.7

Which would be the stronger base, HO^- or NH_3 ?

STRATEGY AND ANSWER: The conjugate acid of the hydroxide ion (HO^-) is H_2O , and water has $\text{p}K_a = 15.7$ (Table 3.1). The conjugate acid of ammonia is the ammonium ion $^+\text{NH}_4$, which has $\text{p}K_a = 9.2$ (meaning it is a stronger acid than water). Since ammonium ion is the stronger acid, its conjugate base NH_3 is the weaker base, and HO^- , the conjugate base of water (the weaker acid), is the stronger base.

PRACTICE PROBLEM 3.8 The $\text{p}K_a$ of the anilinium ion ($\text{C}_6\text{H}_5\text{NH}_3^+$) is 4.63. On the basis of this fact, decide whether aniline ($\text{C}_6\text{H}_5\text{NH}_2$) is a stronger or weaker base than methylamine.

3.6 HOW TO PREDICT THE OUTCOME OF ACID–BASE REACTIONS

Table 3.1 gives the approximate $\text{p}K_a$ values for a range of representative compounds. While you probably will not be expected to memorize all of the $\text{p}K_a$ values in Table 3.1, it is a good idea to begin to learn the general order of acidity and basicity for some of the common acids and bases. The examples given in Table 3.1 are representative of their class or functional group. For example, acetic acid has a $\text{p}K_a = 4.75$, and carboxylic acids generally have $\text{p}K_a$ values near this value (in the range $\text{p}K_a = 3\text{--}5$). Ethyl alcohol is given as an example of an alcohol, and alcohols generally have $\text{p}K_a$ values near that of ethyl alcohol (in the $\text{p}K_a$ range 15–18), and so on. There are exceptions, of course, and we shall learn what these exceptions are as we go on.

By learning the relative scale of acidity of common acids now, you will be able to predict whether or not an acid–base reaction will occur as written.

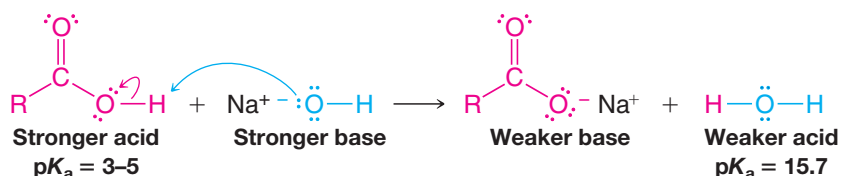
Helpful Hint

Formation of the weaker acid and base is an important general principle for predicting the outcome of acid–base reactions.

- The general principle to apply is this: **acid–base reactions always favor the formation of the weaker acid and the weaker base.**

The reason for this is that the outcome of an acid–base reaction is determined by the position of an equilibrium. Acid–base reactions are said, therefore, to be **under equilibrium control**, and reactions under equilibrium control always favor the formation of the most stable (lowest potential energy) species. The weaker acid and weaker base are more stable (lower in potential energy) than the stronger acid and stronger base.

Using this principle, we can predict that a carboxylic acid (RCO_2H) will react with aqueous NaOH in the following way because the reaction will lead to the formation of the weaker acid (H_2O) and weaker base (RCO_2^-):



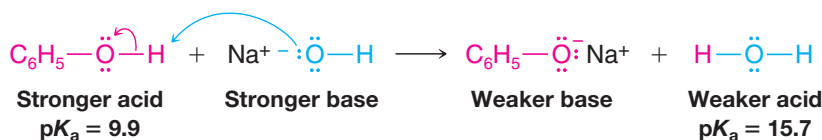
Because there is a large difference in the value of the $\text{p}K_a$ of the two acids, the position of equilibrium will greatly favor the formation of the products. In instances like these we commonly show the reaction with a one-way arrow even though the reaction is an equilibrium.

SOLVED PROBLEM 3.8

Consider the mixing of an aqueous solution of phenol, $\text{C}_6\text{H}_5\text{OH}$ (see Table 3.1), and NaOH . What acid–base reaction, if any, would take place?

STRATEGY: Consider the relative acidities of the reactant (phenol) and of the acid that might be formed (water) by a proton transfer to the base (the hydroxide ion).

ANSWER: The following reaction would take place because it would lead to the formation of a weaker acid (water) from the stronger acid (phenol). It would also lead to the formation of a weaker base, $\text{C}_6\text{H}_5\text{ONa}$, from the stronger base, NaOH .


SOLVED PROBLEM 3.9

Using Table 3.1, explain why the acid–base reaction that takes place between NaH (as source of :H^- ions) and CH_3OH is



rather than



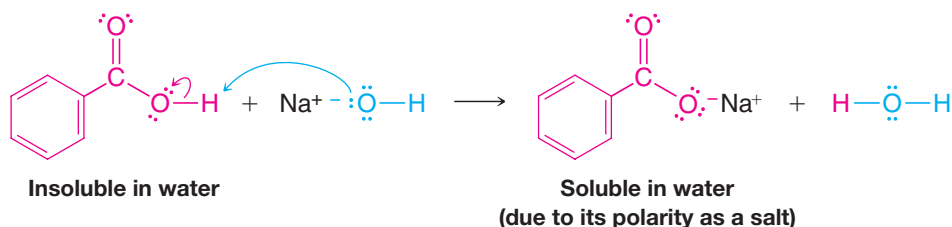
ANSWER: A hydride ion is a very strong base, being the conjugate base of H_2 (a very weak acid, $pK_a = 35$). Hydride will remove the most acidic proton from CH_3OH . Although CH_3OH is not given in Table 3.1, we can compare it to $\text{CH}_3\text{CH}_2\text{OH}$, a similar alcohol whose hydroxyl group pK_a is 16, far more acidic than any proton attached to a carbon without a functional group (e.g., a proton of CH_3CH_3 , which has $pK_a = 50$). Because the proton attached to the oxygen is much more acidic, it is removed preferentially.

Predict the outcome of the following reaction.


PRACTICE PROBLEM 3.9

3.6A Water Solubility as the Result of Salt Formation

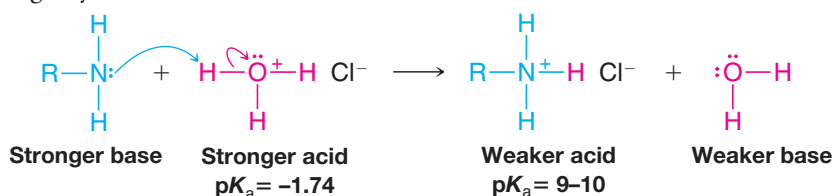
Although acetic acid and other carboxylic acids containing fewer than five carbon atoms are soluble in water, many other carboxylic acids of higher molecular weight are not appreciably soluble in water. Because of their acidity, however, *water-insoluble carboxylic acids dissolve in aqueous sodium hydroxide*; they do so by reacting to form water-soluble sodium salts:



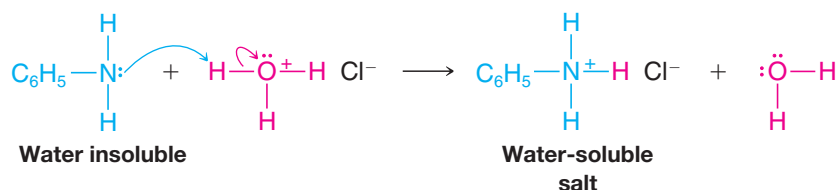


Pseudoephedrine is an amine that is sold as its hydrochloride salt.

We can also predict that an amine will react with aqueous hydrochloric acid in the following way:



While methylamine and most amines of low molecular weight are very soluble in water, amines with higher molecular weights, such as aniline ($\text{C}_6\text{H}_5\text{NH}_2$), have limited water solubility. However, these *water-insoluble amines dissolve readily in hydrochloric acid* because the acid–base reactions convert them into soluble salts:



PRACTICE PROBLEM 3.10 Most carboxylic acids dissolve in aqueous solutions of sodium bicarbonate (NaHCO_3) because, as carboxylate salts, they are more polar. Write curved arrows showing the reaction between a generic carboxylic acid and sodium bicarbonate to form a carboxylate salt and H_2CO_3 . (Note that H_2CO_3 is unstable and decomposes to carbon dioxide and water. You do not need to show that process.)

3.7 RELATIONSHIPS BETWEEN STRUCTURE AND ACIDITY

The strength of a Brønsted–Lowry acid depends on the extent to which a proton can be separated from it and transferred to a base. Removing the proton involves breaking a bond to the proton, and it involves making the conjugate base more electrically negative.

When we compare compounds in a single column of the periodic table, the strength of the bond to the proton is the dominating effect.

- Bond strength to the proton decreases as we move down the column, increasing its acidity.

This phenomenon is mainly due to decreasing effectiveness of orbital overlap between the hydrogen $1s$ orbital and the orbitals of successively larger elements in the column. The less effective the orbital overlap, the weaker is the bond, and the stronger is the acid. The acidities of the hydrogen halides furnish an example:

	pK_a		A c i d i t y i n c r e a s e s ↓
	3.2	H—F	
Group VIIA	–7	H—Cl	
	–9	H—Br	
	–10	H—I	

Helpful Hint

Proton acidity increases as we descend a column in the periodic table due to decreasing bond strength to the proton.

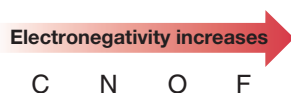
Comparing the hydrogen halides with each other, H—F is the weakest acid and H—I is the strongest. This follows from the fact that the H—F bond is by far the strongest and the H—I bond is the weakest.

Because HI, HBr, and HCl are strong acids, their conjugate bases (I^- , Br^- , Cl^-) are all weak bases. HF, however, is less acidic than the other hydrogen halides and fluoride ion is a stronger base. The fluoride anion is still not nearly as basic as other species we commonly think of as bases, such as the hydroxide anion, however.

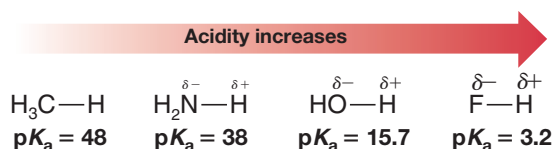
- Acidity increases from left to right when we compare compounds in a given row of the periodic table.

Bond strengths vary somewhat, but the predominant factor becomes the electronegativity of the atom bonded to the hydrogen. The electronegativity of the atom in question affects acidity in two related ways: (1) it affects the polarity of the bond to the proton and (2) it affects the relative stability of the anion (conjugate base) that forms when the proton is lost.

We can see an example of this effect when we compare the acidities of the compounds CH_4 , NH_3 , H_2O , and HF. These compounds are all hydrides of first-row elements, and electronegativity increases across a row of the periodic table from left to right (see Table 1.2):

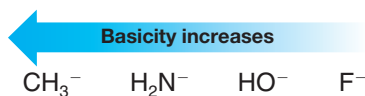


Because fluorine is the most electronegative, the bond in H—F is most polarized, and the proton in H—F is the most positive. Therefore, H—F loses a proton most readily and is the most acidic in this series:



Electrostatic potential maps for these compounds directly illustrate this trend based on electronegativity and increasing polarization of the bonds to hydrogen (Fig. 3.2). Almost no positive charge (indicated by the extent of color trending toward blue) is evident at the hydrogens of methane. Very little positive charge is present at the hydrogens of ammonia. This is consistent with the weak electronegativity of both carbon and nitrogen and hence with the behavior of methane and ammonia as exceedingly weak acids ($\text{p}K_{\text{a}}$ values of 48 and 38, respectively). Water shows significant positive charge at its hydrogens ($\text{p}K_{\text{a}}$ more than 20 units lower than ammonia), and hydrogen fluoride clearly has the highest amount of positive charge at its hydrogen ($\text{p}K_{\text{a}}$ of 3.2), resulting in strong acidity.

Because H—F is the strongest acid in this series, its conjugate base, the fluoride ion (F^-), will be the weakest base. Fluorine is the most electronegative atom and it accommodates the negative charge most readily:



The methanide ion (CH_3^-) is the least stable anion of the four, because carbon being the least electronegative element is least able to accept the negative charge. The methanide ion, therefore, is the strongest base in this series. [The methanide ion, a **carbanion**, and the amide ion ($^-\text{NH}_2$) are exceedingly strong bases because they are the conjugate bases of extremely weak acids. We shall discuss some uses of these powerful bases in Section 3.14.]

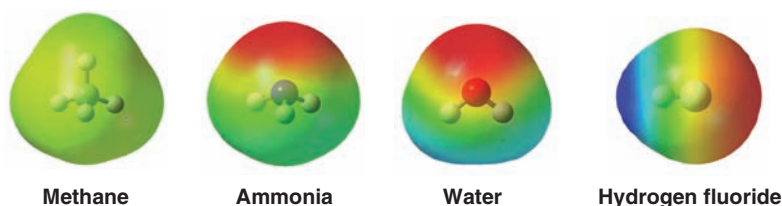


FIGURE 3.2 The effect of increasing electronegativity among elements from left to right in the first row of the periodic table is evident in these maps of electrostatic potential for methane, ammonia, water, and hydrogen fluoride.

Helpful Hint

Proton acidity increases from left to right in a given row of the periodic table due to increasing stability of the conjugate base.

FIGURE 3.3 A summary of periodic trends in relative acidity. Acidity increases from left to right across a given row (electronegativity effect) and from top to bottom in a given column (bond strength effect) of the periodic table.

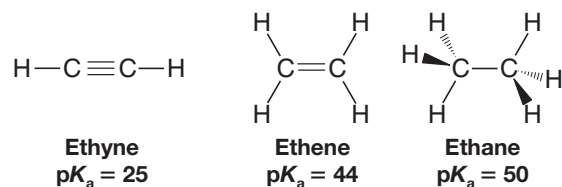
	Acidity increases within a given row (electronegativity effect)				
					Acidity increases within a given column (bond strength effect)
Hydride pK_a	C (H ₃ C—H) 48	N (H ₂ N—H) 38	O (HO—H) 15.7	F (F—H) 3.2	
			S (HS—H) 7.0	Cl (Cl—H) -7	
			Se (HSe—H) 3.9	Br (Br—H) -9	
				I (I—H) -10	

Trends in acidity within the periodic table are summarized in Fig. 3.3.

3.7A The Effect of Hybridization

- An alkyne hydrogen is weakly acid. Alkene and alkane hydrogens are essentially not acidic.

The pK_a values for ethyne, ethene, and ethane illustrate this trend.



We can explain this order of acidities on the basis of the hybridization state of carbon in each compound. Electrons of $2s$ orbitals have lower energy than those of $2p$ orbitals because *electrons in $2s$ orbitals tend, on the average, to be much closer to the nucleus than electrons in $2p$ orbitals.* (Consider the shapes of the orbitals: $2s$ orbitals are spherical and centered on the nucleus; $2p$ orbitals have lobes on either side of the nucleus and are extended into space.)

- With hybrid orbitals, **having more s character means that the electrons of the anion will, on the average, be lower in energy, and the anion will be more stable.**

The sp orbitals of the C—H bonds of ethyne have 50% s character (because they arise from the combination of one s orbital and one p orbital), those of the sp^2 orbitals of ethene have 33.3% s character, while those of the sp^3 orbitals of ethane have only 25% s character. This means, in effect, that the sp carbon atoms of ethyne act as if they were more electronegative than the sp^2 carbon atoms of ethene and the sp^3 carbon atoms of ethane. (Remember: electronegativity measures an atom's ability to hold bonding electrons close to its nucleus, and having electrons closer to the nucleus makes it more stable.)

- An sp carbon atom is effectively more electronegative than an sp^2 carbon, which in turn is more electronegative than an sp^3 carbon.

The effect of hybridization and effective electronegativity on acidity is borne out in the calculated electrostatic potential maps for ethyne, ethene, and ethane shown in Fig. 3.4. Some positive charge (indicated by blue color) is clearly evident on the hydrogens of ethyne ($pK_a = 25$), but almost no positive charge is present on the hydrogens of ethene and ethane (both having pK_a values more than 20 units greater than ethyne).

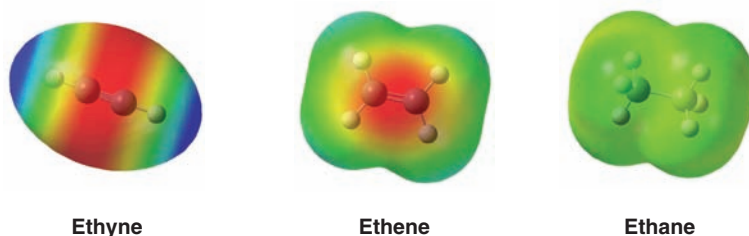
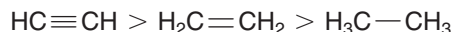


FIGURE 3.4 Electrostatic potential maps for ethyne, ethene, and ethane.

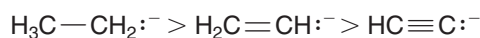
In summary, the order of relative acidities of ethyne, ethene, and ethane parallels the effective electronegativity of the carbon atom in each compound:

Relative Acidity of the Hydrocarbons



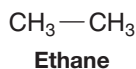
As expected based on the properties of acid–base conjugate pairs, an sp^3 carbanion is the strongest base in a series based on carbon hybridization, and an sp carbanion (an alkynide) is the weakest base. This trend is illustrated here with the conjugate bases of ethane, ethene, and ethyne.

Relative Basicity of the Carbanions



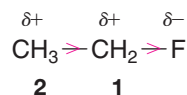
3.7B Inductive Effects

The carbon–carbon bond of ethane is completely nonpolar because at each end of the bond there are two identical methyl groups:



The C—C bond is nonpolar.

This is not the case with the carbon–carbon bond of ethyl fluoride, however:



One end of the bond, the one nearer the fluorine atom, is more negative than the other. This polarization of the carbon–carbon bond results from an intrinsic electron-attracting ability of the fluorine (because of its electronegativity) that is transmitted *through space* and *through the bonds of the molecule*. Chemists call this kind of effect an inductive effect.

- **Inductive effects** are electronic effects transmitted through bonds. The inductive effect of a group can be **electron donating** or **electron withdrawing**. Inductive effects weaken as the distance from the group increases.

In the case of ethyl fluoride, the positive charge that the fluorine imparts to C1 is greater than that imparted to C2 because the fluorine is closer to C1.

Figure 3.5 shows the dipole moment for ethyl fluoride (fluoroethane). The distribution of negative charge around the electronegative fluorine is plainly evident in the calculated electrostatic potential map.

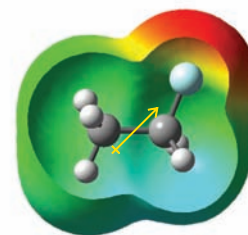


FIGURE 3.5 Ethyl fluoride, showing its dipole moment inside a cutaway view of the electrostatic potential at its van der Waals surface.

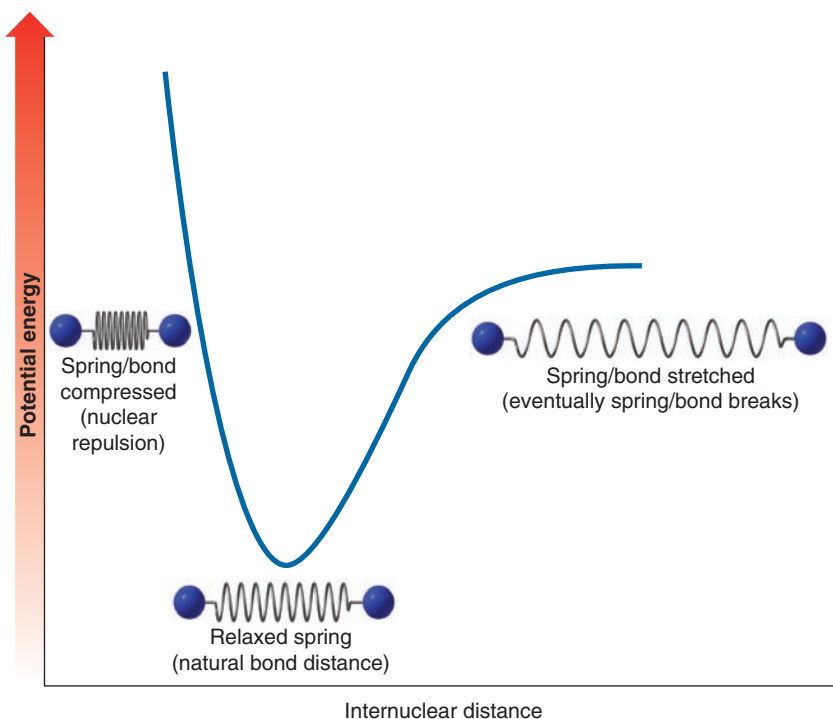
3.8 ENERGY CHANGES

Energy is defined as the capacity to do work. The two fundamental types of energy are **kinetic energy** and **potential energy**.

Kinetic energy is the energy an object has because of its motion; it equals one-half the object's mass multiplied by the square of its velocity (i.e., $\frac{1}{2}mv^2$).

Potential energy is stored energy. It exists only when an attractive or repulsive force exists between objects. Two balls attached to each other by a spring (an analogy

FIGURE 3.6 Potential energy exists between objects that either attract or repel each other. In the case of atoms joined by a covalent bond, or objects connected by a spring, the lowest potential energy state occurs when atoms are at their ideal internuclear distance (bond length), or when a spring between objects is relaxed. Lengthening or shortening the bond distance, or compressing or stretching a spring, raises the potential energy.



we used for covalent bonds when we discussed infrared spectroscopy in Section 2.15) can have their potential energy increased when the spring is stretched or compressed (Fig. 3.6). If the spring is stretched, an attractive force will exist between the balls. If it is compressed, a repulsive force will exist. In either instance releasing the balls will cause the potential energy (stored energy) of the balls to be converted into kinetic energy (energy of motion).

Chemical energy is a form of potential energy. It exists because attractive and repulsive electrical forces exist between different pieces of the molecules. Nuclei attract electrons, nuclei repel each other, and electrons repel each other.

It is usually impractical (and often impossible) to describe the *absolute* amount of potential energy contained by a substance. Thus we usually think in terms of its *relative potential energy*. We say that one system has *more* or *less* potential energy than another.

Another term that chemists frequently use in this context is the term **stability** or **relative stability**. *The relative stability of a system is inversely related to its relative potential energy.*

- **The more potential energy an object has, the less stable it is.**

Consider, as an example, the relative potential energy and the relative stability of snow when it lies high on a mountainside and when it lies serenely in the valley below. Because of the attractive force of gravity, the snow high on the mountain *has greater potential energy and is much less stable* than the snow in the valley. This greater potential energy of the snow on the mountainside can become converted into the enormous kinetic energy of an avalanche. By contrast, the snow in the valley, with its lower potential energy and with its greater stability, is incapable of releasing such energy.

3.8A Potential Energy and Covalent Bonds

Atoms and molecules possess potential energy—often called chemical energy—that can be released as heat when they react. Because heat is associated with molecular motion, this release of heat results from a change from potential energy to kinetic energy.

From the standpoint of covalent bonds, the state of greatest potential energy is the state of free atoms, the state in which the atoms are not bonded to each other at all. This is true because the formation of a chemical bond is always accompanied by the lowering

of the potential energy of the atoms (cf. Fig. 1.8). Consider as an example the formation of hydrogen molecules from hydrogen atoms:



The potential energy of the atoms decreases by 436 kJ mol^{-1} as the covalent bond forms. This potential energy change is illustrated graphically in Fig. 3.7.

A convenient way to represent the relative potential energies of molecules is in terms of their relative **enthalpies**, or **heat contents**, H . (*Enthalpy* comes from *en* + *thalpein*, Greek: to heat.) The difference in relative enthalpies of reactants and products in a chemical change is called the **enthalpy change** and is symbolized by ΔH° . [The Δ (delta) in front of a quantity usually means the difference, or change, in the quantity. The superscript $^\circ$ indicates that the measurement is made under standard conditions.]

By convention, the sign of ΔH° for **exothermic reactions** (those evolving heat) is negative. **Endothermic reactions** (those that absorb heat) have a positive ΔH° . The heat of reaction, ΔH° , measures the change in enthalpy of the atoms of the reactants as they are converted to products. For an exothermic reaction, the atoms have a smaller enthalpy as products than they do as reactants. For endothermic reactions, the reverse is true.

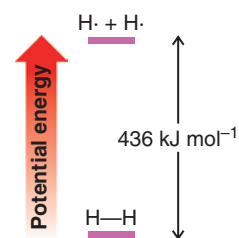


FIGURE 3.7 The relative potential energies of hydrogen atoms and a hydrogen molecule.

3.9 THE RELATIONSHIP BETWEEN THE EQUILIBRIUM CONSTANT AND THE STANDARD FREE-ENERGY CHANGE, ΔG°

An important **relationship exists between the equilibrium constant (K_{eq}) and the standard free-energy change (ΔG°)**, for a reaction.[†]

$$\Delta G^\circ = -RT \ln K_{\text{eq}}$$

where R is the gas constant and equals $8.314 \text{ J K}^{-1} \text{ mol}^{-1}$ and T is the absolute temperature in kelvins (K).

This equation tells us the following:

- **For a reaction to favor the formation of products when equilibrium is reached it must have a negative value for ΔG° .** Free energy must be *lost* as the reactants become products; that is, the reaction must go down an energy hill. For such a reaction the equilibrium constant will be greater than one. If ΔG° is more negative than 13 kJ mol^{-1} the equilibrium constant will be large enough for the reaction to *go to completion*, meaning that more than 99% of the reactants will be converted to products when equilibrium is reached.
- **For reactions with a positive ΔG° , the formation of products at equilibrium is unfavorable.** The equilibrium constant for these reactions will be less than one.

The free-energy change (ΔG°) has two components, the **enthalpy change** (ΔH°) and the **entropy change** (ΔS°). The relationship between these three thermodynamic quantities is

$$\Delta G^\circ = \Delta H^\circ - T \Delta S^\circ$$

We have seen (Section 3.8) that ΔH° is associated with changes in bonding that occur in a reaction. If, collectively, stronger bonds are formed in the products than existed in the starting materials, then ΔH° will be negative (i.e., the reaction is *exothermic*). If the reverse is true, then ΔH° will be positive (the reaction is *endothermic*). **A negative value for ΔH° , therefore, will contribute to making ΔG° negative and will consequently**

*The unit of energy in SI units is the joule, J, and $1 \text{ cal} = 4.184 \text{ J}$. (Thus $1 \text{ kcal} = 4.184 \text{ kJ}$.) A kilocalorie of energy (1000 cal) is the amount of energy in the form of heat required to raise by 1°C the temperature of 1 kg (1000 g) of water at 15°C .

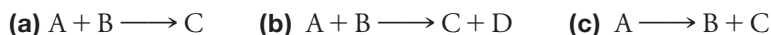
[†]By standard free-energy change (ΔG°), we mean that the products and reactants are taken as being in their standard states (1 atm of pressure for a gas and 1 M for a solution). The free-energy change is often called the **Gibbs free-energy change**, to honor the contributions to thermodynamics of J. Willard Gibbs, a professor of mathematical physics at Yale University in the latter part of the nineteenth century.

favor the formation of products. For the ionization of an acid, the less positive or more negative the value of ΔH° , the stronger the acid will be.

Entropy changes have to do with *changes in the relative order of a system*. **The more random a system is, the greater is its entropy.** Therefore, a positive entropy change ($+\Delta S^\circ$) is always associated with a change from a more ordered system to a less ordered one. A negative entropy change ($-\Delta S^\circ$) accompanies the reverse process. In the equation $\Delta G^\circ = \Delta H^\circ - T \Delta S^\circ$, the entropy change (multiplied by T) is preceded by a negative sign; this means that **a positive entropy change (from order to disorder) makes a negative contribution to ΔG° and is energetically favorable for the formation of products.**

For many reactions in which the number of molecules of products equals the number of molecules of reactants (e.g., when two molecules react to produce two molecules), the entropy change will be small. This means that except at high temperatures (where the term $T \Delta S^\circ$ becomes large even if ΔS° is small) the value of ΔH° will largely determine whether or not the formation of products will be favored. If ΔH° is large and negative (if the reaction is exothermic), then the reaction will favor the formation of products at equilibrium. If ΔH° is positive (if the reaction is endothermic), then the formation of products will be unfavorable.

PRACTICE PROBLEM 3.11 State whether you would expect the entropy change, ΔS° , to be positive, negative, or approximately zero for each of the following reactions. (Assume the reactions take place in the gas phase.)

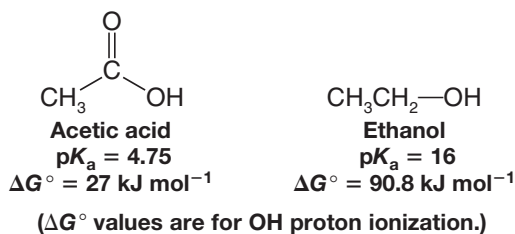


PRACTICE PROBLEM 3.12 (a) What is the value of ΔG° for a reaction where $K_{\text{eq}} = 1$? (b) Where $K_{\text{eq}} = 10$? (The change in ΔG° required to produce a 10-fold increase in the equilibrium constant is a useful term to remember.) (c) Assuming that the entropy change for this reaction is negligible (or zero), what change in ΔH° is required to produce a 10-fold increase in the equilibrium constant?

3.10 ACIDITY: CARBOXYLIC ACIDS VERSUS ALCOHOLS

Carboxylic acids are weak acids, typically having $\text{p}K_{\text{a}}$ values in the range of 3–5. Alcohols, by comparison, have $\text{p}K_{\text{a}}$ values in the range of 15–18, and essentially do not give up a proton unless exposed to a very strong base.

To understand the reasons for this difference, let's consider acetic acid and ethanol as representative examples of simple carboxylic acids and alcohols.



Using the $\text{p}K_{\text{a}}$ for acetic acid (4.75), one can calculate (Section 3.9) that the free-energy change (ΔG°) for ionization of the carboxyl proton of acetic acid is $+27 \text{ kJ mol}^{-1}$, a moderately endergonic (unfavorable) process, since the ΔG° value is positive. Using the $\text{p}K_{\text{a}}$ of ethanol (16), one can calculate that the corresponding free-energy change for ionization of the hydroxyl proton of ethanol is $+90.8 \text{ kJ mol}^{-1}$, a much more endergonic (and hence even less favorable) process. These calculations reflect the fact that ethanol

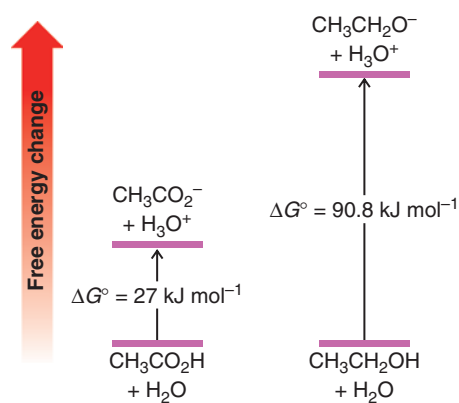
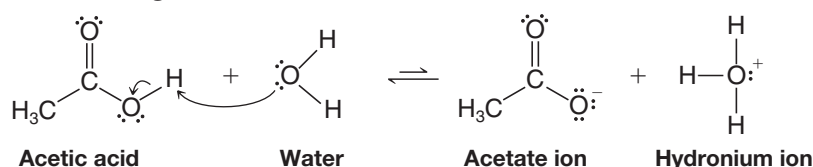


FIGURE 3.8 A diagram comparing the free-energy changes that accompany ionization of acetic acid and ethanol. Ethanol has a larger positive free-energy change and is a weaker acid because its ionization is more unfavorable.

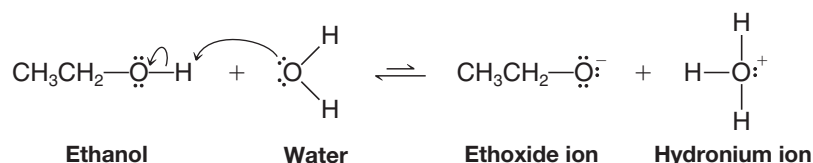
is much less acidic than acetic acid. Figure 3.8 depicts the magnitude of these energy changes in a relative sense.

How do we explain the much greater acidity of carboxylic acids than alcohols? Consider first the structural changes that occur if both acetic acid and ethanol act as acids by donating a proton to water.

Acetic Acid Acting as an Acid



Ethanol Acting as an Acid

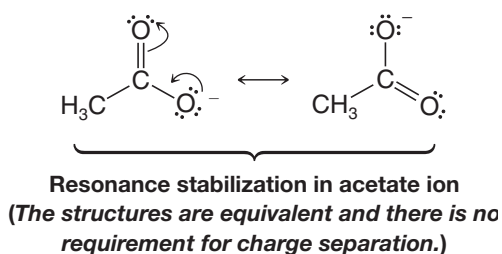


What we need to focus on is the relative stability of the conjugate bases derived from a carboxylic acid and an alcohol. This is because the smaller free-energy change for ionization of a carboxylic acid (e.g., acetic acid) as compared to an alcohol (e.g., ethanol) has been attributed to greater stabilization of the negative charge in the carboxylate ion as compared to an alkoxide ion. Greater stabilization of the carboxylate ion appears to arise from two factors: (a) delocalization of charge (as depicted by resonance structures for the carboxylate ion, Section 3.10A), and (b) an inductive electron-withdrawing effect (Section 3.7B).

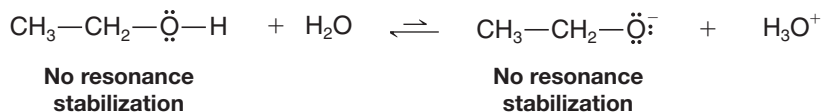
3.10A The Effect of Delocalization

Delocalization of the negative charge is possible in a carboxylate anion, but it is not possible in an alkoxide ion. We can show how delocalization is possible in carboxylate ions by writing **resonance** structures for the acetate ion.

Two Resonance Structures That Can Be Written for Acetate Anion

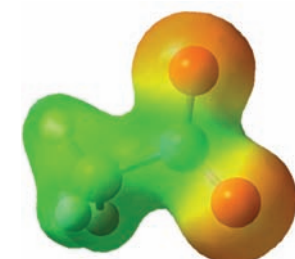


The two resonance structures we drew above distributed the negative charge to both oxygen atoms of the carboxylate group, thereby stabilizing the charge. This is a **delocalization effect** (by resonance). In contrast, no resonance structures are possible for an alkoxide ion, such as ethoxide. (You may wish to review the rules we have given in Section 1.8 for writing proper resonance structures.)

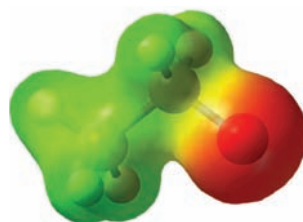


No resonance structures can be drawn for either ethanol or ethoxide anion.

A rule to keep in mind is that **charge delocalization is always a stabilizing factor**, and because of charge stabilization, the energy difference for formation of a carboxylate ion from a carboxylic acid is less than the energy difference for formation of an alkoxide ion from an alcohol. Since the energy difference for ionization of a carboxylic acid is less than for an alcohol, the carboxylic acid is a stronger acid.



Acetate anion



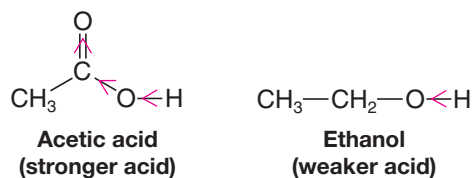
Ethoxide anion

FIGURE 3.9 Calculated electrostatic potential maps at a surface approximating the bonding electron density for acetate anion and ethoxide anion. Although both molecules carry the same -1 net charge, acetate stabilizes the charge better by dispersing it over both oxygen atoms.

3.10B The Inductive Effect

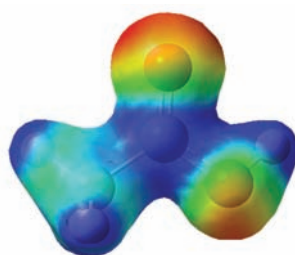
We have already shown how the negative charge in a carboxylate ion can be delocalized over two oxygen atoms by resonance. However, the electronegativity of these oxygen atoms further helps to stabilize the charge, by what is called an **inductive electron-withdrawing effect**. A carboxylate ion has two oxygen atoms whose combined electronegativity stabilizes the charge more than in an alkoxide ion, which has only a single electronegative oxygen atom. In turn, this lowers the energy barrier to forming the carboxylate ion, making a carboxylic acid a stronger acid than an alcohol. This effect is evident in electrostatic potential maps depicting approximately the bonding electron density for the two anions (Fig. 3.9). Negative charge in the acetate anion is evenly distributed over the two oxygen atoms, whereas in ethoxide the negative charge is localized on its sole oxygen atom (as indicated by red in the electrostatic potential map).

It is also reasonable to expect that a carboxylic acid would be a stronger acid than an alcohol when considering each as a neutral molecule (i.e., prior to loss of a proton), because both functional groups have a highly polarized O—H bond, which in turn weakens the bond to the hydrogen atom. However, the significant electron-withdrawing effect of the carbonyl group in acetic acid and the absence of an adjacent electron-withdrawing group in ethanol make the carboxylic acid hydrogen much more acidic than the alcohol hydrogen.

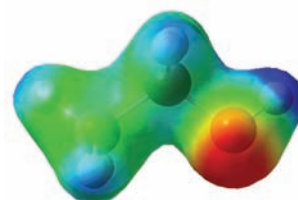


Electrostatic potential maps at approximately the bond density surface for acetic acid and ethanol (Fig. 3.10) clearly show the positive charge at the carbonyl carbon of acetic acid, as compared to the CH_2 carbon of ethanol.

FIGURE 3.10 Maps of electrostatic potential at approximately the bond density surface for acetic acid and ethanol. The positive charge at the carbonyl carbon of acetic acid is evident in the blue color of the electrostatic potential map at that position, as compared to the hydroxyl carbon of ethanol. The inductive electron-withdrawing effect of the carbonyl group in carboxylic acids contributes to the acidity of this functional group.



Acetic acid



Ethanol

3.10C Summary and a Comparison of Conjugate Acid–Base Strengths

In summary, the greater acidity of a carboxylic acid is predominantly due to the ability of its conjugate base (a carboxylate ion) to stabilize a negative charge better than an alkoxide ion, the conjugate base of an alcohol. In other words, the conjugate base of a carboxylic acid is a weaker base than the conjugate base of an alcohol. Therefore, since there is an inverse strength relationship between an acid and its conjugate base, a carboxylic acid is a stronger acid than an alcohol.

Helpful Hint

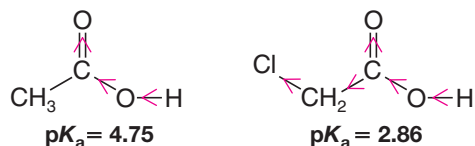
The more stable a conjugate base is, the stronger the corresponding acid.

Draw contributing resonance structures and a hybrid resonance structure that explain two related facts: the carbon–oxygen bond distances in the acetate ion are the same, and the oxygens of the acetate ion bear equal negative charges.

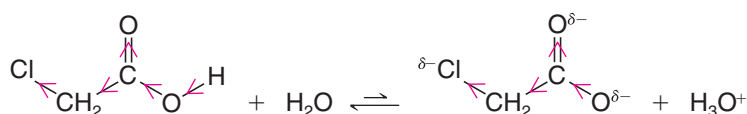
PRACTICE PROBLEM 3.13

3.10D Inductive Effects of Other Groups

The acid-strengthening effect of other electron-attracting groups (other than the carbonyl group) can be shown by comparing the acidities of acetic acid and chloroacetic acid:



This is an example of a **substituent effect**. The greater acidity of chloroacetic acid can be attributed, in part, to the extra electron-attracting inductive effect of the electronegative chlorine atom. By adding its inductive effect to that of the carbonyl group and the oxygen, it makes the hydroxyl proton of chloroacetic acid even more positive than that of acetic acid. It also stabilizes the chloroacetate ion that is formed when the proton is lost *by dispersing its negative charge* (Fig. 3.11):



Dispersal of charge always makes a species more stable, and, as we have seen now in several instances, **any factor that stabilizes the conjugate base of an acid increases the strength of the acid**. (In Section 3.11, we shall see that entropy changes in the solvent are also important in explaining the increased acidity of chloroacetic acid.)

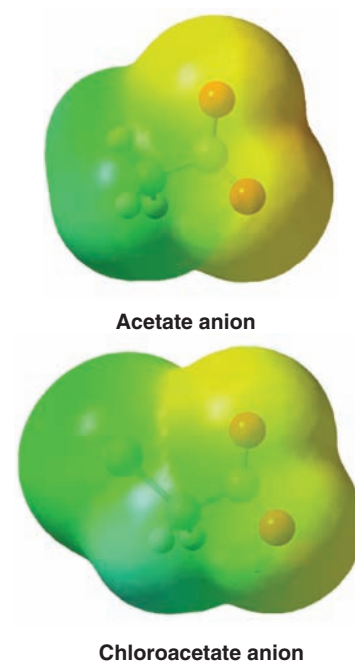
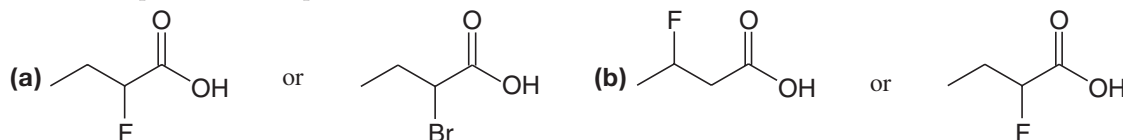


FIGURE 3.11 The electrostatic potential maps for acetate and chloroacetate ions show the relatively greater ability of chloroacetate to disperse the negative charge.

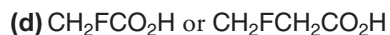
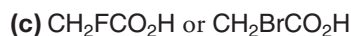
SOLVED PROBLEM 3.10

Which compound in each pair would be most acidic?



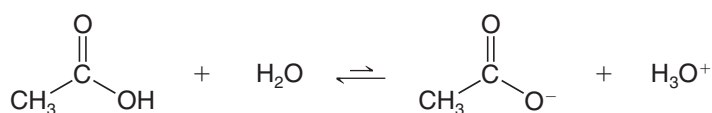
STRATEGY AND ANSWER: Decide what is similar in each pair and what is different. In pair (a), the difference is the halogen substituent on the carbon adjacent to the carboxyl group. In the first example it is fluorine; in the second it is bromine. Fluorine is much more electronegative (electron-attracting) than bromine (Table 1.2); therefore it will be able to disperse the negative charge of the anion formed when the proton is lost. Thus the first compound will be the stronger acid. In pair (b), the difference is the position of the fluorine substituents. In the second compound the fluorine is closer to the carboxyl group where it will be better able to disperse the negative charge in the anion formed when the proton is lost. The second compound will be the stronger acid.

PRACTICE PROBLEM 3.14 Which would you expect to be the stronger acid? Explain your reasoning in each instance.



3.11 THE EFFECT OF THE SOLVENT ON ACIDITY

In the absence of a solvent (i.e., in the gas phase), most acids are far weaker than they are in solution. In the gas phase, for example, acetic acid is estimated to have a $\text{p}K_a$ of about 130 (a K_a of $\sim 10^{-130}$)! The reason is this: when an acetic acid molecule donates a proton to a water molecule in the gas phase, the ions that are formed are oppositely charged particles and the particles must become separated:



In the absence of a solvent, separation is difficult. In solution, solvent molecules surround the ions, insulating them from one another, stabilizing them, and making it far easier to separate them than in the gas phase.

In a solvent such as water, called a protic solvent, solvation by hydrogen bonding is important (Section 2.13D).

- A **protic solvent** is one that has a hydrogen atom attached to a strongly electronegative element such as oxygen or nitrogen.

A protic solvent, therefore, can form hydrogen bonds to the unshared electron pairs of an acid and its conjugate base, but they may not stabilize both equally.

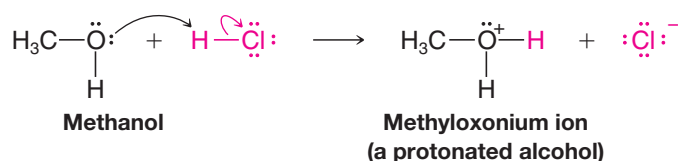
- The stability of a conjugate base is enhanced if it is solvated to a greater extent than the corresponding acid.

Relative acidity cannot be predicted solely on the basis of solvation, however. Steric factors affecting solvation, and the relative order or disorder of the solvent molecules (entropic parameters), can enhance or decrease acidity.

3.12 ORGANIC COMPOUNDS AS BASES

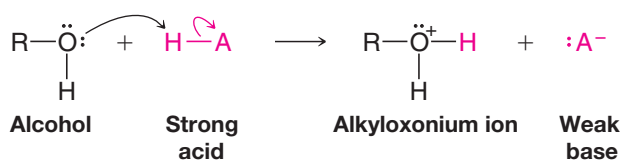
If an organic compound contains an atom with an unshared electron pair, it is a potential base. We saw in Section 3.5C that compounds with an unshared electron pair on a nitrogen atom (i.e., amines) act as bases. Let us now consider several examples in which organic compounds having an unshared electron pair on an oxygen atom act in the same way.

Dissolving gaseous HCl in methanol brings about an acid–base reaction much like the one that occurs with water (Section 3.1A):

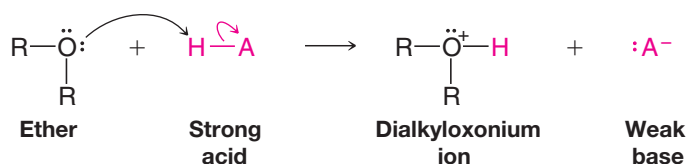


The conjugate acid of the alcohol is often called a **protonated alcohol**, although more formally it is called an **alkyloxonium ion** or simply an **oxonium ion**.

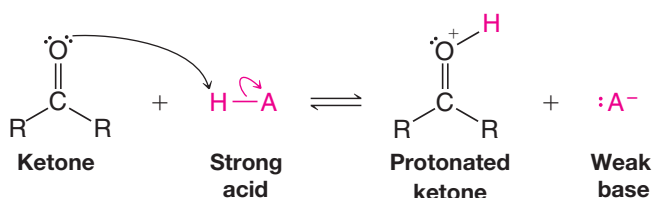
Alcohols, in general, undergo this same reaction when they are treated with solutions of strong acids such as HCl, HBr, HI, and H₂SO₄:



So, too, do ethers:

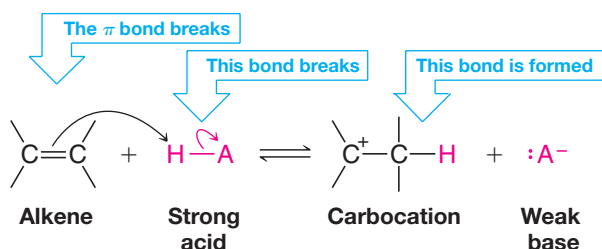


Compounds containing a carbonyl group also act as bases in the presence of a strong acid:



Proton transfer reactions like these are often the first step in many reactions that alcohols, ethers, aldehydes, ketones, esters, amides, and carboxylic acids undergo. The p*K*_a values for some of these protonated intermediates are given in Table 3.1.

An atom with an unshared electron pair is not the only locus that confers basicity on an organic compound. The π bond of an alkene can have the same effect. Later we shall study many reactions in which, as a first step, alkenes react with a strong acid by accepting a proton in the following way:



In this reaction the electron pair of the π bond of the alkene is used to form a bond between one carbon of the alkene and the proton donated by the strong acid. Notice that two bonds are broken in this process: the π bond of the double bond and the bond between the proton of the acid and its conjugate base. One new bond is formed: a bond between a carbon of the alkene and the proton. This process leaves the other carbon of the alkene trivalent, electron deficient, and with a formal positive charge. A compound containing a carbon of this type is called a **carbocation** (Section 3.4). As we shall see in later chapters, carbocations are unstable intermediates that react further to produce stable molecules.

It is a general rule that any organic compound containing oxygen, nitrogen, or a multiple bond will dissolve in concentrated sulfuric acid. Explain the basis of this rule in terms of acid–base reactions and intermolecular forces.

Helpful Hint

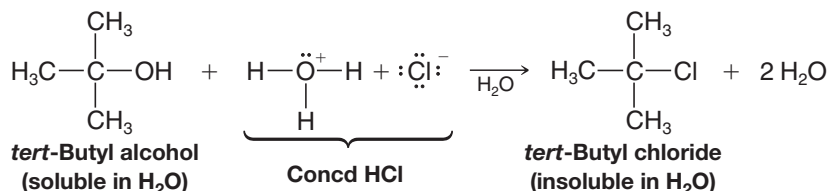
Proton transfers are a common first step in many reactions we shall study.

PRACTICE PROBLEM 3.15

3.13 A MECHANISM FOR AN ORGANIC REACTION

In Chapter 6 we shall begin our study of organic **reaction mechanisms** in earnest. Let us consider now one mechanism as an example, one that allows us to apply some of the chemistry we have learned in this chapter and one that, at the same time, will reinforce what we have learned about how curved arrows are used to illustrate mechanisms.

Dissolving *tert*-butyl alcohol in concentrated (concd) aqueous hydrochloric acid soon results in the formation of *tert*-butyl chloride. The reaction is a **substitution reaction**:

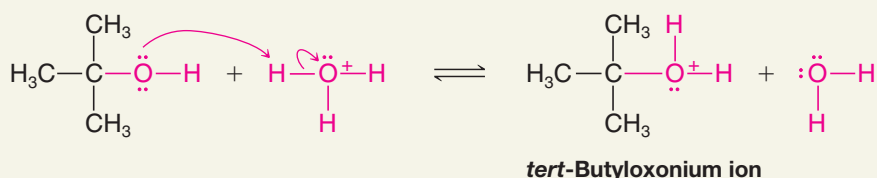


That a reaction has taken place is obvious when one actually does the experiment. *tert*-Butyl alcohol is soluble in the aqueous medium; however, *tert*-butyl chloride is not, and consequently it separates from the aqueous phase as another layer in the flask. It is easy to remove this nonaqueous layer, purify it by distillation, and thus obtain the *tert*-butyl chloride.

Considerable evidence, described later, indicates that the reaction occurs in the following way.

A MECHANISM FOR THE REACTION — Reaction of *tert*-Butyl Alcohol with Concentrated Aqueous HCl

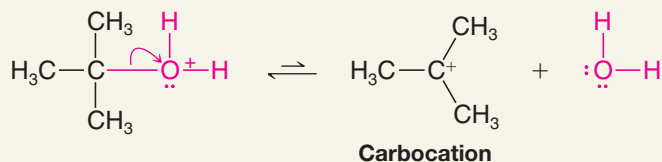
Step 1



tert-Butyl alcohol acts as a base and accepts a proton from the hydronium ion. (Chloride anions are spectators in this step of the reaction.)

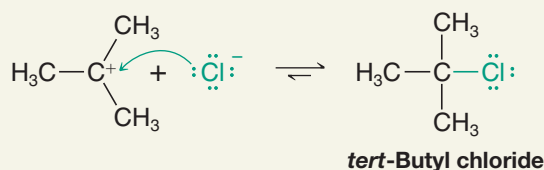
The products are a protonated alcohol and water (the conjugate acid and base).

Step 2



The bond between the carbon and oxygen of the *tert*-butyloxonium ion breaks heterolytically, leading to the formation of a carbocation and a molecule of water.

Step 3



The carbocation, acting as a Lewis acid, accepts an electron pair from a chloride ion to become the product.

Notice that **all of these steps involve acid–base reactions**. Step 1 is a straightforward Brønsted acid–base reaction in which the alcohol oxygen removes a proton from the hydronium ion. Step 2 is the reverse of a Lewis acid–base reaction. In it, the carbon–oxygen bond of the protonated alcohol breaks heterolytically as a water molecule departs with the electrons of the bond. This happens, in part, because the alcohol is protonated. The presence of a formal positive charge on the oxygen of the protonated alcohol weakens the carbon–oxygen bond by drawing the electrons in the direction of the positive oxygen. Step 3 is a Lewis acid–base reaction, in which a chloride anion (a Lewis base) reacts with the carbocation (a Lewis acid) to form the product.

A question might arise: why doesn't a molecule of water (also a Lewis base) instead of a chloride ion react with the carbocation? After all, there are many water molecules around, since water is the solvent. The answer is that this step does occur sometimes, but it is simply the reverse of step 2. That is to say, not all of the carbocations that form go on directly to become product. Some react with water to become protonated alcohols again. However, these will dissociate again to become carbocations (even if, before they do, they lose a proton to become the alcohol again). Eventually, however, most of them are converted to the product because, under the conditions of the reaction, the equilibrium of the last step lies far to the right, and the product separates from the reaction mixture as a second phase.

3.14 ACIDS AND BASES IN NONAQUEOUS SOLUTIONS

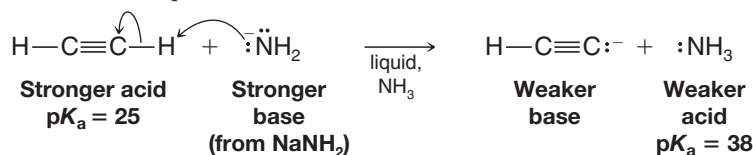
If you were to add sodium amide (NaNH_2) to water in an attempt to carry out a reaction using the amide ion (NH_2^-) as a very powerful base, the following reaction would take place immediately:



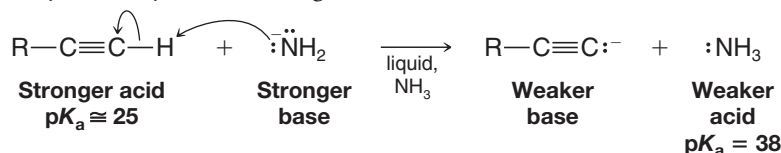
The amide ion would react with water to produce a solution containing hydroxide ion (a much weaker base) and ammonia. This example illustrates what is called the **leveling effect of the solvent**. Water, the solvent here, *donates a proton to any base stronger than a hydroxide ion*. Therefore, *it is not possible to use a base stronger than hydroxide ion in aqueous solution*.

We can use bases stronger than hydroxide ion, however, if we choose solvents that are weaker acids than water. We can use amide ion (e.g., from NaNH_2) in a solvent such as hexane, diethyl ether, or liquid NH_3 (the liquified gas, bp -33°C , not the aqueous solution that you may have used in your general chemistry laboratory). All of these solvents are very weak acids (we generally don't think of them as acids), and therefore they will not donate a proton even to the strong base NH_2^- .

We can, for example, convert ethyne to its conjugate base, a carbanion, by treating it with sodium amide in liquid ammonia:



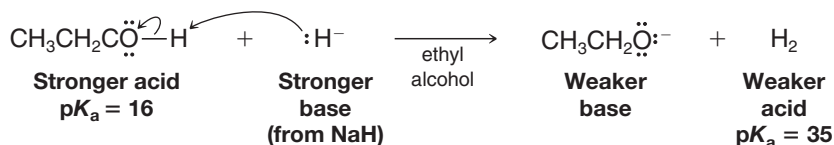
Most **terminal alkynes** (alkynes with a proton attached to a triply bonded carbon) have pK_a values of about 25; therefore, all react with sodium amide in liquid ammonia in the same way that ethyne does. The general reaction is



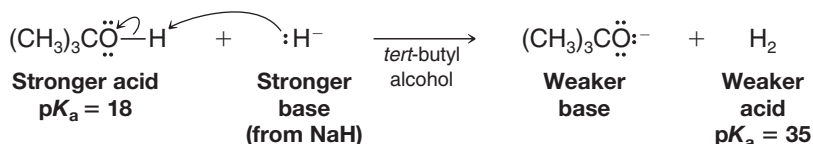
Helpful Hint

We shall use this reaction as part of our introduction to organic synthesis in Chapter 7.

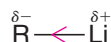
Alcohols are often used as solvents for organic reactions because, being somewhat less polar than water, they dissolve less polar organic compounds. Using alcohols as solvents also offers the advantage of using RO^- ions (called **alkoxide ions**) as bases. Alkoxide ions are somewhat stronger bases than hydroxide ions because alcohols are weaker acids than water. For example, we can create a solution of sodium ethoxide ($\text{CH}_3\text{CH}_2\text{ONa}$) in ethyl alcohol by adding sodium hydride (NaH) to ethyl alcohol. We use a large excess of ethyl alcohol because we want it to be the solvent. Being a very strong base, the hydride ion reacts readily with ethyl alcohol:



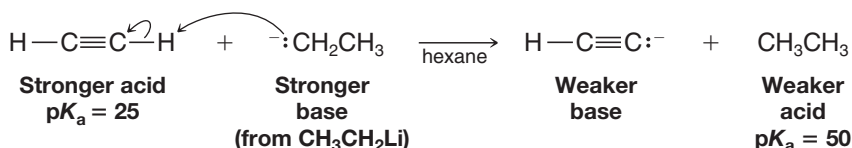
The *tert*-butoxide ion, $(\text{CH}_3)_3\text{CO}^-$, in *tert*-butyl alcohol, $(\text{CH}_3)_3\text{COH}$, is a stronger base than the ethoxide ion in ethyl alcohol, and it can be prepared in a similar way:



Although the carbon–lithium bond of an alkyllithium (RLi) has covalent character, it is polarized so as to make the carbon negative:



Alkyllithium reagents react as though they contain alkanide (R^-) ions and, being the conjugate bases of alkanes, alkanide ions are the strongest bases that we shall encounter. Ethyllithium ($\text{CH}_3\text{CH}_2\text{Li}$), for example, acts as though it contains an ethanide (CH_3CH_2^-) carbanion. It reacts with ethyne in the following way:



Alkyllithiums can be easily prepared by allowing an alkyl bromide to react with lithium metal in an ether solvent (such as diethyl ether). See Section 12.6.

PRACTICE PROBLEM 3.16

Write equations for the acid–base reaction that would occur when each of the following compounds or solutions are mixed. In each case label the stronger acid and stronger base, and the weaker acid and weaker base, by using the appropriate pK_a values (Table 3.1). If no appreciable acid–base reaction would occur, you should indicate this.

- | | |
|---|--|
| (a) NaH is added to CH_3OH . | (d) NH_4Cl is added to sodium amide in liquid ammonia. |
| (b) NaNH_3 is added to $\text{CH}_3\text{CH}_2\text{OH}$. | (e) $(\text{CH}_3)_3\text{CONa}$ is added to H_2O . |
| (c) Gaseous NH_2 is added to ethyllithium in hexane. | (f) NaOH is added to $(\text{CH}_3)_3\text{COH}$. |

3.15 ACID–BASE REACTIONS AND THE SYNTHESIS OF DEUTERIUM- AND TRITIUM-LABELED COMPOUNDS

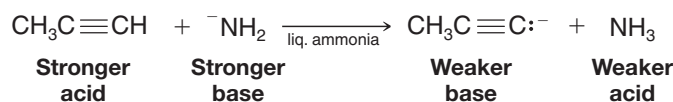
Chemists often use compounds in which deuterium or tritium atoms have replaced one or more hydrogen atoms of the compound as a method of “labeling” or identifying particular hydrogen atoms. Deuterium (^2H) and tritium (^3H) are isotopes of hydrogen with masses of 2 and 3 atomic mass units (amu), respectively.

One way to introduce a deuterium or tritium atom into a specific location in a molecule is through the acid–base reaction that takes place when a very strong base is treated with D_2O or T_2O (water that has deuterium or tritium in place of its hydrogens). For example, treating a solution containing $(CH_3)_2CHLi$ (isopropyllithium) with D_2O results in the formation of propane labeled with deuterium at the central atom:

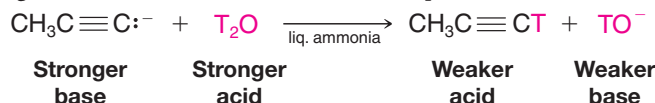

SOLVED PROBLEM 3.11

Assuming you have available propyne, a solution of sodium amide in liquid ammonia, and T_2O , show how you would prepare the tritium-labeled compound $CH_3C\equiv CT$.

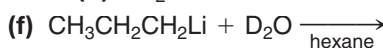
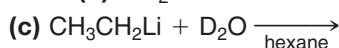
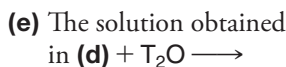
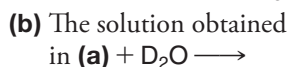
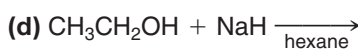
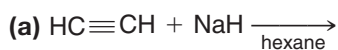
ANSWER: First add propyne to sodium amide in liquid ammonia. The following acid–base reaction will take place:



Then adding T_2O (a much stronger acid than NH_3) to the solution will produce $CH_3C\equiv CT$:



Complete the following acid–base reactions:


PRACTICE PROBLEM 3.17

3.16 APPLICATIONS OF BASIC PRINCIPLES

Again we review how certain basic principles apply to topics we have studied in this chapter.

Electronegativity Differences Polarize Bonds We saw how this principle applies to the heterolysis of bonds to carbon in Section 3.4 and in explaining the strength of acids in Sections 3.7 and 3.10B.

Polarized Bonds Underlie Inductive Effects In Section 3.10B we saw how polarized bonds explain effects that we call *inductive effects* and how these effects are part of the explanation for why carboxylic acids are more acidic than corresponding alcohols.

Opposite Charges Attract This principle is fundamental to understanding *Lewis acid–base theory* as we saw in Section 3.3A. Positively charged centers in molecules that are electron pair acceptors are attracted to negatively charged centers in electron pair donors. In Section 3.4 we saw this principle again in the reaction of carbocations (positively charged Lewis acids) with anions (which are negatively charged by definition) and other Lewis bases.

Nature Prefers States of Lower Potential Energy In Section 3.8A we saw how this principle explains the energy changes—called *enthalpy changes*—that take place when covalent bonds form, and in Section 3.9 we saw the role enthalpy changes play in explaining how large or how small the equilibrium constant for a reaction is. The

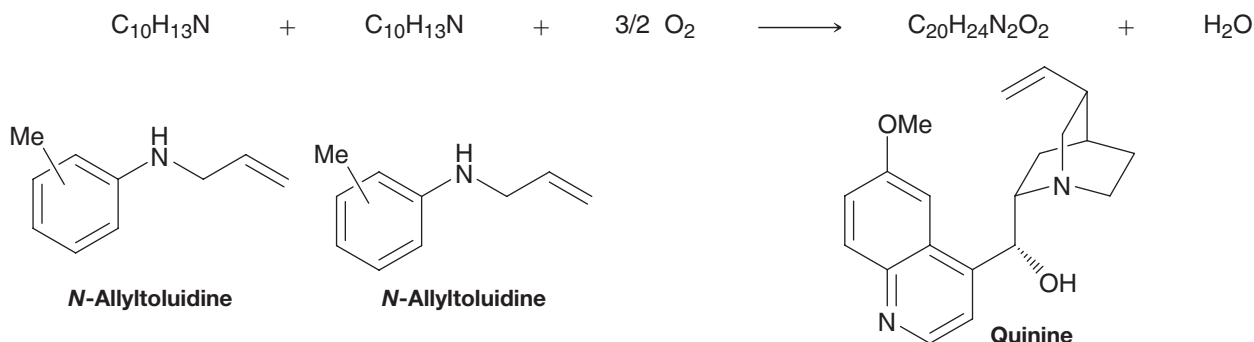
lower the potential energy of the products, the larger is the equilibrium constant, and the more favored is the formation of the products when equilibrium is reached. This section also introduced a related principle: **Nature prefers disorder to order**—or, to put it another way, a *positive entropy change* for a reaction favors the formation of the products at equilibrium.

Resonance Effects Can Stabilize Molecules and Ions When a molecule or ion can be represented by two or more equivalent resonance structures, then the molecule or ion will be stabilized (will have its potential energy lowered) by delocalization of charge. In Section 3.10A we saw how this effect helps explain the greater acidity of carboxylic acids when compared to corresponding alcohols.

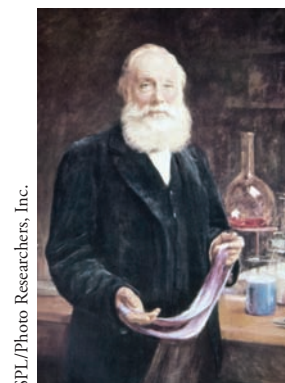
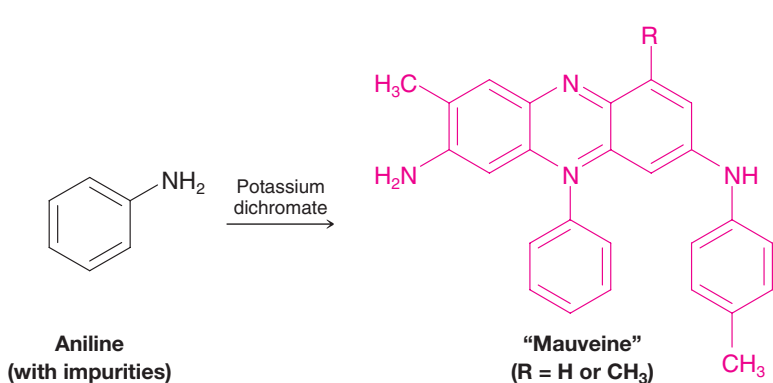
WHY Do These Topics Matter?]

THE RARITY OF CHEMICAL DISCOVERIES WITHOUT KNOWLEDGE OF THE MECHANISMS

From the time of its initial discovery in the 1630s until the middle of the twentieth century, the natural product quinine was the world's only real treatment for malaria. Yet, because it could only be obtained in small quantities from relatively remote places of the globe, it was a medicine that effectively was available to only a small number of very wealthy or well-connected individuals. In light of this issue, scientists began to wonder whether quinine could be synthesized in the laboratory, an idea that was first put to the test in 1856 by a graduate student in England named William Henry Perkin. Perkin's plan for synthesis was based on an idea posited in 1849 by his mentor, August Wilhelm von Hofmann, that quinine could be prepared from the constituents of coal tar. This notion was based on the balanced chemical equation shown below. The formulas were all that was known at the time, not the actual structures. We realize today that there was no chance for success in this endeavor simply because there is no mechanism by which these chemicals could react in the right way. Fortune, however, sometimes arrives in unexpected ways.



Perkin did his most important experiment on this problem in a laboratory at his family home, an experiment in which he altered his supervisor's idea ever so slightly by using a different starting material (aniline, containing several different contaminants) and heating it in the presence of a strong oxidant (potassium dichromate). What resulted was a dark tar that looked a bit like asphalt. Although such products are often the result of reactions gone wrong, Perkin attempted to see if he could get anything in the tarry residue to dissolve by adding different solvents. Some did nothing, but when he added ethanol, a beautiful purple-colored solution was formed. This solution proved capable of turning any light-colored fabric the exact same purple shade. Although not quinine, what Perkin had discovered was the first synthetic dye, a way to color fabric a shade previously reserved for royalty. Indeed, before Perkin's discovery, the only way to obtain a purple-colored dye was by the tedious isolation of mucous secretions of select Mediterranean snails.



W. H. Perkin

Perkin ended up making a fortune from his discovery, a material he called mauveine, which is actually composed of two compounds. The more important outcome, however, was that it showed for the first time that organic chemistry could really change the world, launching an entire industry of other chemists looking to make ever more fanciful and wonderful colors not readily found in nature.

The key message, though, is that no matter how wonderful this story is, it is only one of a handful of cases in which there was such a significant outcome in the absence of any real chemical knowledge of mechanism. Major discoveries are much more likely when it is known what the given compounds might actually do when they react together! Otherwise, organic chemistry would be just alchemy. That might explain why it took nearly another century of work before quinine actually succumbed to laboratory synthesis.

To learn more about these topics, see:

1. Garfield, S. *Mauve: How One Man Invented a Color that Changed the World*. Faber and Faber, **2001**, p. 240.
2. Nicolaou, K. C.; Montagnon, T. *Molecules that Changed the World*. Wiley-VCH: Weinheim, **2008**, p. 366.
3. Meth-Cohn, O; Smith, M. "What did W. D. Perkin actually make when he oxidised aniline to obtain mauveine?", *J. Chem. Soc. Perkin Trans 1*, **1994**, 5–7.

SUMMARY AND REVIEW TOOLS

In Chapter 3 you studied acid–base chemistry, one of the most important topics needed to learn organic chemistry. If you master acid–base chemistry you will be able to understand most of the reactions that you study in organic chemistry, and by understanding how reactions work, you will be able to learn and remember them more easily.

You have reviewed the Brønsted–Lowry definition of acids and bases and the meanings of pH and pK_a . You have learned to identify the most acidic hydrogen atoms in a molecule based on a comparison of pK_a values. You will see in many cases that Brønsted–Lowry acid–base reactions either initiate or complete an organic reaction, or prepare an organic molecule for further reaction. The Lewis definition of acids and bases may have been new to you. However, you will see over and over again that Lewis acid–base reactions which involve either the donation of an electron pair to form a new covalent bond or the departure of an electron pair to break a covalent bond are central steps in many organic reactions. The vast majority of organic reactions you will study are either Brønsted–Lowry or Lewis acid–base reactions.

Your knowledge of organic structure and polarity from Chapters 1 and 2 has been crucial to your understanding of acid–base reactions. You have seen that stabilization of charge by delocalization is key to determining how readily an acid will give up a proton, or how readily a base will accept a proton. In addition, you have learned the essential skill of drawing curved arrows to accurately show the movement of electrons in these processes. With these concepts and skills you will be prepared to understand how organic reactions occur on a step-by-step basis—something organic chemists call “a mechanism for the reaction.”

So, continue to work hard to master acid–base chemistry and other fundamentals. Your toolbox is quickly filling with the tools you need for overall success in organic chemistry!

The study aids for this chapter include key terms and concepts (which are hyperlinked to the glossary from the bold, blue terms in the *WileyPLUS* version of the book at wileyplus.com) and a Concept Map after the end-of-chapter problems.

PROBLEMS

Note to Instructors: Many of the homework problems are available for assignment via *WileyPLUS*, an online teaching and learning solution.

BRØNSTED–LOWRY ACIDS AND BASES

3.18 What is the conjugate base of each of the following acids?

- (a) NH_3 (b) H_2O (c) H_2 (d) $\text{HC}\equiv\text{CH}$ (e) CH_3OH (f) H_3O^+

3.19 List the bases you gave as answers to Exercise 3.18 in order of decreasing basicity.

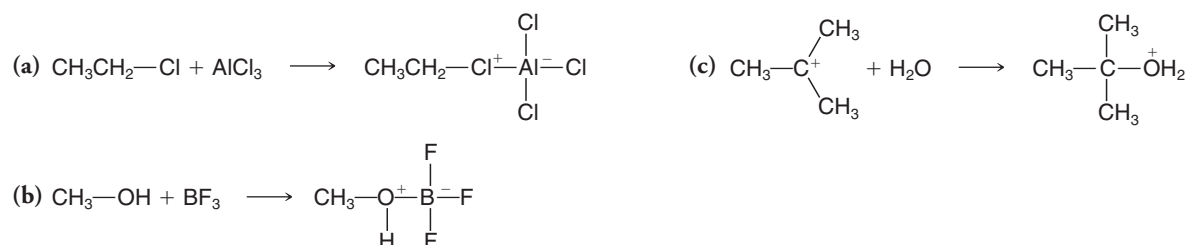
3.20 What is the conjugate acid of each of the following bases?

- (a) HSO_4^- (b) H_2O (c) CH_3NH_2 (d) $^-\text{NH}_2$ (e) $\text{CH}_3\bar{\text{C}}\text{H}_2$ (f) CH_3CO_2^-

3.21 List the acids you gave as answers to Exercise 3.20 in order of decreasing acidity.

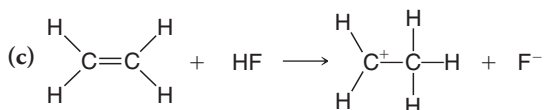
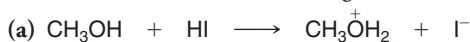
LEWIS ACIDS AND BASES

3.22 Designate the Lewis acid and Lewis base in each of the following reactions:

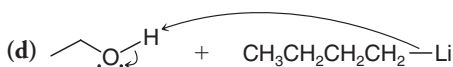
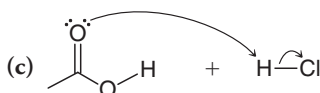
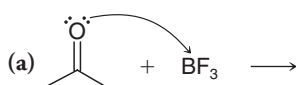


CURVED-ARROW NOTATION

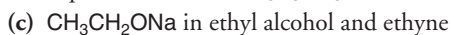
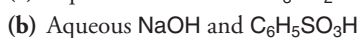
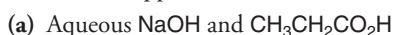
3.23 Rewrite each of the following reactions using curved arrows and show all nonbonding electron pairs:



3.24 Follow the curved arrows and write the products.



3.25 Write an equation, using the curved-arrow notation, for the acid–base reaction that will take place when each of the following are mixed. If no appreciable acid–base reaction takes place, because the equilibrium is unfavorable, you should so indicate.



ACID–BASE STRENGTH AND EQUILIBRIA

3.26 When methyl alcohol is treated with NaH, the product is $\text{CH}_3\text{O}^-\text{Na}^+$ (and H_2) and not $\text{Na}^+\text{CH}_2\text{OH}$ (and H_2). Explain why this is so.

3.27 What reaction will take place if ethyl alcohol is added to a solution of $\text{HC}\equiv\text{C}^-\text{Na}^+$ in liquid ammonia?

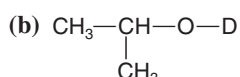
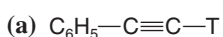
3.28 (a) The K_a of formic acid (HCO_2H) is 1.77×10^{-4} . What is the $\text{p}K_a$? (b) What is the K_a of an acid whose $\text{p}K_a = 13$?

3.29 Acid HA has $\text{p}K_a = 20$; acid HB has $\text{p}K_a = 10$.

(a) Which is the stronger acid?

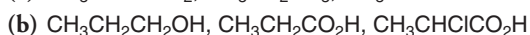
(b) Will an acid–base reaction with an equilibrium lying to the right take place if Na^+A^- is added to HB? Explain your answer.

3.30 Starting with appropriate unlabeled organic compounds, show syntheses of each of the following:

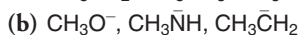
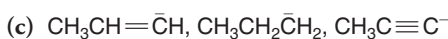
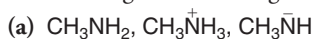


3.31 (a) Arrange the following compounds in order of decreasing acidity and explain your answer: $\text{CH}_3\text{CH}_2\text{NH}_2$, $\text{CH}_3\text{CH}_2\text{OH}$, and $\text{CH}_3\text{CH}_2\text{CH}_3$. (b) Arrange the conjugate bases of the acids given in part (a) in order of increasing basicity and explain your answer.

3.32 Arrange the following compounds in order of decreasing acidity:



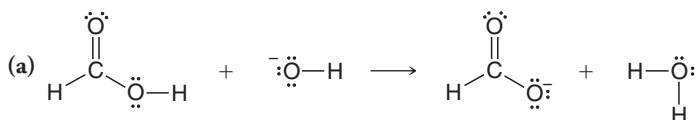
3.33 Arrange the following in order of increasing basicity:

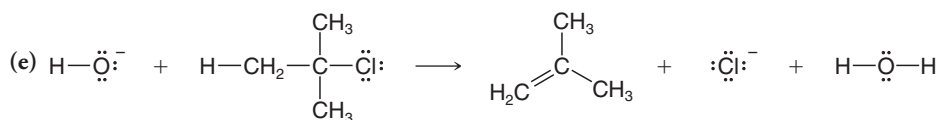
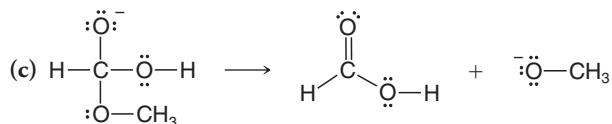
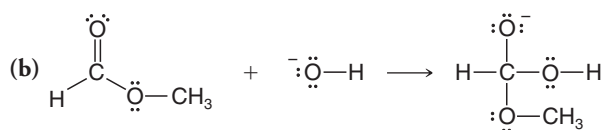


GENERAL PROBLEMS

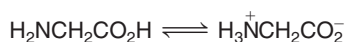
3.34 Whereas H_3PO_4 is a triprotic acid, H_3PO_3 is a diprotic acid. Draw structures for these two acids that account for this difference in behavior.

3.35 Supply the curved arrows necessary for the following reactions:





3.36 Glycine is an amino acid that can be obtained from most proteins. In solution, glycine exists in equilibrium between two forms:



(a) Consult Table 3.1 and state which form is favored at equilibrium.

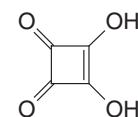
(b) A handbook gives the melting point of glycine as 262 °C (with decomposition). Which of the structures given above best represents glycine?

3.37 Malonic acid, $HO_2CCH_2CO_2H$, is a diprotic acid. The pK_a for the loss of the first proton is 2.83; the pK_a for the loss of the second proton is 5.69. (a) Explain why malonic acid is a stronger acid than acetic acid ($pK_a = 4.75$). (b) Explain why the anion, $^-O_2CCH_2CO_2H$, is so much less acidic than malonic acid itself.

3.38 The free-energy change, ΔG° , for the ionization of acid HA is 21 kJ mol⁻¹; for acid HB it is -21 kJ mol⁻¹. Which is the stronger acid?

3.39 At 25 °C the enthalpy change, ΔH° , for the ionization of trichloroacetic acid is +6.3 kJ mol⁻¹ and the entropy change, ΔS° , is +0.0084 kJ mol⁻¹ K⁻¹. What is the pK_a of trichloroacetic acid?

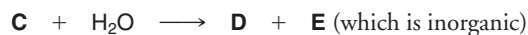
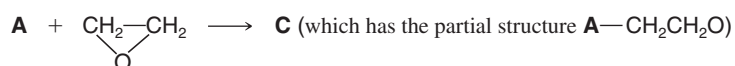
3.40 The compound at right has (for obvious reasons) been given the trivial name **squaric acid**. Squaric acid is a diprotic acid, with both protons being more acidic than acetic acid. In the dianion obtained after the loss of both protons, all of the carbon-carbon bonds are the same length as well as all of the carbon-oxygen bonds. Provide a resonance explanation for these observations.



Squaric acid

CHALLENGE PROBLEMS

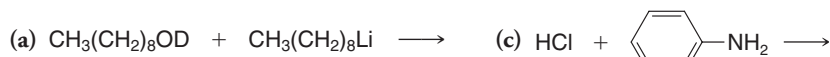
3.41 $CH_3CH_2SH + CH_3O^- \longrightarrow A$ (contains sulfur) + **B**



(a) Given the above sequence of reactions, draw structures for **A** through **E**.

(b) Rewrite the reaction sequence, showing all nonbonding electron pairs and using curved arrows to show electron pair movements.

3.42 First, complete and balance each of the equations below. Then, choosing among ethanol, hexane, and liquid ammonia, state which (there may be more than one) might be suitable solvents for each of these reactions. Disregard the practical limitations that come from consideration of "like dissolves like" and base your answers only on relative acidities.



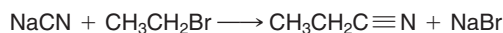
(The conjugate acid of this amine, aniline, has a pK_a of 4.63.)

3.43 Dimethylformamide (DMF), $HCON(CH_3)_2$, is an example of a polar aprotic solvent, aprotic meaning it has no hydrogen atoms attached to highly electronegative atoms.

(a) Draw its dash structural formula, showing unshared electron pairs.

(b) Draw what you predict to be its most important resonance forms [one is your answer to part (a)].

(c) DMF, when used as the reaction solvent, greatly enhances the reactivity of nucleophiles (e.g., ^-CN from sodium cyanide) in reactions like this:

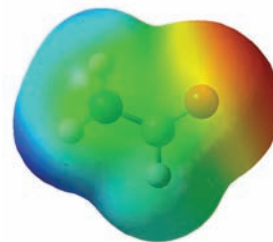


Suggest an explanation for this effect of DMF on the basis of Lewis acid-base considerations. (*Hint*: Although water or an alcohol solvates both cations and anions, DMF is only effective in solvating cations.)

3.44 As noted in Table 3.1, the pK_a of acetone, CH_3COCH_3 , is 19.2.

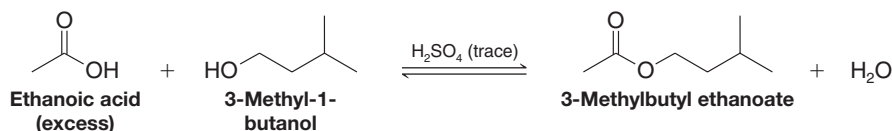
- Draw the bond-line formula of acetone and of any other contributing resonance form.
- Predict and draw the structure of the conjugate base of acetone and of any other contributing resonance form.
- Write an equation for a reaction that could be used to synthesize $\text{CH}_3\text{COCH}_2\text{D}$.

3.45 Formamide (HCONH_2) has a pK_a of approximately 25. Predict, based on the map of electrostatic potential for formamide shown here, which hydrogen atom(s) has this pK_a value. Support your conclusion with arguments having to do with the electronic structure of formamide.



LEARNING GROUP PROBLEMS

Suppose you carried out the following synthesis of 3-methylbutyl ethanoate (isoamyl acetate):

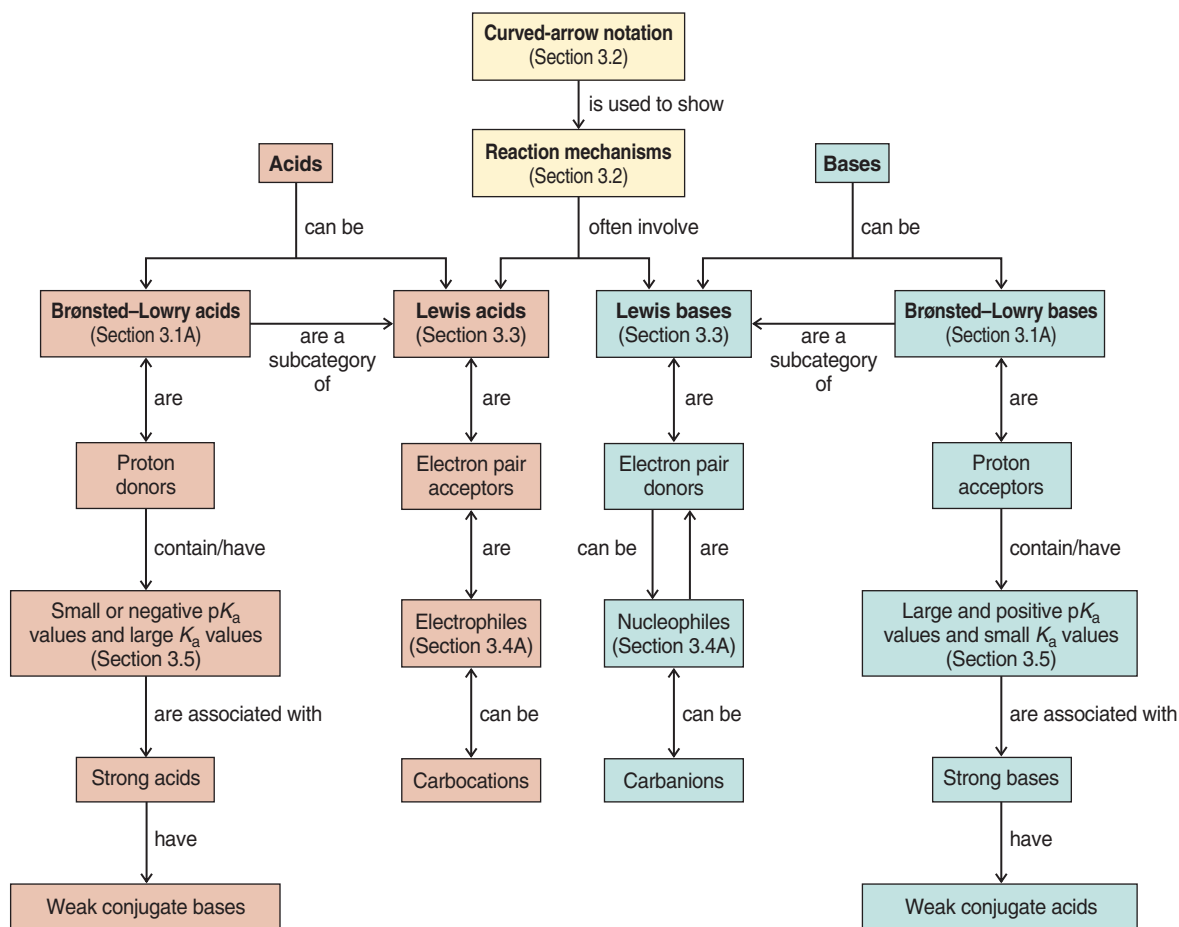


As the chemical equation shows, 3-methyl-1-butanol (also called isoamyl alcohol or isopentyl alcohol) was mixed with an excess of acetic acid (ethanoic acid by its systematic name) and a trace of sulfuric acid (which serves as a catalyst). This reaction is an equilibrium reaction, so it is expected that not all of the starting materials will be consumed. The equilibrium should lie quite far to the right due to the excess of acetic acid used, but not completely.

After an appropriate length of time, isolation of the desired product from the reaction mixture was begun by adding a volume of 5% aqueous sodium bicarbonate (NaHCO_3 has an effective pK_a of 7) roughly equal to the volume of the reaction mixture. Bubbling occurred and a mixture consisting of two layers resulted—a basic aqueous layer and an organic layer. The layers were separated and the aqueous layer was removed. The addition of aqueous sodium bicarbonate to the layer of organic materials and separation of the layers were repeated twice. Each time the predominantly aqueous layers were removed, they were combined in the same collection flask. The organic layer that remained after the three bicarbonate extractions was dried and then subjected to distillation in order to obtain a pure sample of 3-methylbutyl ethanoate (isoamyl acetate).

- List all the chemical species likely to be present at the end of the reaction but before adding aqueous NaHCO_3 . Note that the H_2SO_4 was not consumed (since it is a catalyst), and is thus still available to donate a proton to atoms that can be protonated.
- Use a table of pK_a values, such as Table 3.1, to estimate pK_a values for any potentially acidic hydrogens in each of the species you listed in part 1 (or for the conjugate acid).
- Write chemical equations for all the acid–base reactions you would predict to occur (based on the pK_a values you used) when the species you listed above encounter the aqueous sodium bicarbonate solution. (*Hint:* Consider whether each species might be an acid that could react with NaHCO_3 .)
- Explain, on the basis of polarities and solubility, why separate layers formed when aqueous sodium bicarbonate was added to the reaction mixture. (*Hint:* Most sodium salts of organic acids are soluble in water, as are neutral oxygen-containing organic compounds of four carbons or less.)
 - List the chemical species likely to be present after the reaction with NaHCO_3 in (i) the organic layer and (ii) the aqueous layer.
 - Why was the aqueous sodium bicarbonate extraction step repeated three times?

[CONCEPT MAP]



With respect to the conjugate base

